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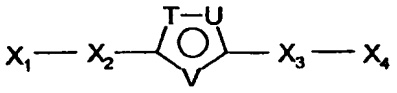

(I)

(57) Abstract

The present invention relates to novel compounds of formula (I) wherein X_1, X_2, X_3, X_4, T, U and V have the meanings provided. The invention further relates to combinatorial libraries containing at least two or more such compounds, and to methods of preparing combinatorial libraries composed of such compounds.

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OXADIAZOLE, THIADIAZOLE AND TRIAZOLE DERIVATIVES AND COMBINATORIAL LIBRARIES THEREOF

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

The present invention relates generally to the synthesis of compounds comprising heterocyclic rings. In one specific embodiment, the invention provides novel oxadiazoles as well as novel combinatorial libraries comprised of such compounds.

BACKGROUND INFORMATION

The process of discovering new therapeutically active compounds for a given indication involves the screening of all compounds from available compound collections. From the compounds tested one or more structure(s) is selected as a promising lead. A large number of related analogs are then synthesized in order to develop a structure-activity relationship and select one or more optimal compounds. With traditional "one-at-a-time" synthesis and biological testing of analogs, this optimization process is long and labor intensive. Adding significant numbers of new structures to the compound collections used in the initial screening step of the discovery and optimization process cannot be accomplished with traditional "one-at-a-time" synthesis methods, except over a time frame of years or even decades. Faster methods are needed that allow for the preparation of up to thousands of related compounds in a matter of days or a few weeks. This need is particularly evident when it comes to synthesizing more complex compounds, such as oxadiazoles.

Solid-phase techniques for the synthesis of peptides have been extensively developed and combinatorial libraries of peptides have been generated with great success. During the past four years there has been substantial development of chemically synthesized combinatorial libraries (SCLs) made up of peptides. The preparation and use of synthetic peptide combinatorial libraries has been described, for example, by Houghten et al., (*Proc. Natl. Acad. Sci. USA* 1985, 82, 5131; Biochemistry, 1993, 32, 11035; and U.S. Patent No. 4,631,211) utilized individual polyethylene bags, referred to "tea bags" to generate peptide libraries. The tea bags, containing C-terminal amino acids bound to a solid support, were mixed and coupled with the requisite amino acids using solid phase synthesis techniques. Common steps, such as resin washing and deprotection of a-amino groups, can be performed simultaneously in a single reaction vessel and upon completion of the synthesis, each bag contained a single peptide sequence. Dooley et al. in U.S. Patent 5,367,053, used combinatorial libraries for the determination of high affinity opioid receptors. Huebner in U.S. Patent 5,182,366, describes a method of preparing a mixture of peptides having known composition using three essential steps, dividing an amount of a mixture of amino acid derivatized resins, coupling a subsequent amino acid and combining a known amount of a different resin together to obtain peptide mixtures. Also described are methods to retrieve and analyze the amino acid sequence. Appel et al. in WO PCT 92/09300, describes the synthesis of complex mixtures of solid support-coupled amino acids in which the mixture contains an equimolar representation of each reacted amino acid coupled. Geysen in published European Patent Application 0 138 855 describes a method of synthesizing a peptide library and detecting a peptide comprising a sequence of

amino acids which has antigenic activity. Pirrung et al. in U.S. Patent 5,143,854 describe polypeptide arrays synthesized using photoremovable groups. Synthesized combinatorial libraries have provided an extraordinary number of various peptides in such libraries and the availability of rapid screening of the library which can identify lead pharmaceutical peptides.

Combinatorial approaches have recently been extended to "organic," or non-peptide, libraries. Zambias et al. (U.S. Patent No. 5,712,171) describe a method of generating libraries that contain aminimides, oxazolones, sulfonylaminides and phosphonylaminides as the core structure in spatially arranged arrays. Combinatorial chemical methods have been applied to a limited number of heterocyclic compounds, as described, for example, in U.S. Patent Nos. 5,288,514; 5,324,483; and Goff et al., *J. Org. Chem.*, 60:5748-5749 (1995). See also U.S.Patent Nos. 5,549,974 and 5,506,337. However, the heterocyclic libraries to date contain compounds of limited diversity and complexity.

Substituent limitations have been overcome for mixtures of peptides and peptidomimetics through the use of solid phase techniques versus solution-phase. An important step in the development of solid-phase techniques was the discovery of methods to prepare large numbers of individual compounds simultaneously, as described, for example, by Houghten in U.S. Patent No. 4,631,211. These solid phase methods, however, have rarely been applied to the syntheses of complex heterocyclic structures. Therefore a need exists to develop more complex "organic" libraries based on heterocyclic medicinal compounds which would need less time and effort in the synthesis and testing required to bring an organic pharmaceutical product to fruition. In short, improved methods for generating therapeutically

useful heterocyclic compounds, such as oxadiazole and thiadiazole derivatives, are desired.

Oxadiazoles, for example, have been the subject of investigation in a number of different biological areas. A number of patents cite oxadiazole derivatives as pesticides and acaricides. 1,2,4-Oxadiazoles have been proposed as: (a) muscarinic receptor agonists (as described by Messer W. S. Jr., et al., *J. Med. Chem.* 40:1230 (1997); Showell, G. A., et al., *J. Med. Chem.*, 34:1086 (1991); Orlek, B. S., et al., *J. Med. Chem.*, 34: 2726 (1991)), (b) benzodiazepine receptor agonists (as described by Watjen, F., et al. *J. Med. Chem.*, 32:2282 (1989)), (c) histamine H_3 receptor antagonists (as described by Clitherow, J. W.; et al. *Bioorg. Med. Chem. Lett.*, 6: 833 (1996)), and (d) antiviral compounds (as described by Diana, G. D., et al. *J. Med. Chem.*, 37:2421 (1994)). In general, the oxadiazole ring system has been used as a replacement for ester or amide functionalities and has been primarily limited to simpler alkyl and aryl derivatives (Andersen, K. E., et al. *Eur. J. Med. Chem.*, 31:417 (1996)). A series of dipeptidomimetic oxadiazoles have been made and incorporated into peptide sequences as replacements for dipeptides (Borg, S., et al., *Proc. Am. Pept. Symp., 14th*, 689-690, (Mayflower Scientific, Kingswinford, UK 1996); Borg, S., et al. *J. Org. Chem.*, 60:3112 (1996); Borg, S., et al. *Eur. J. Med. Chem.* 28: 801 (1993)). Oxadiazoles with a 5-chloromethyl substituent have been described as plant growth regulators (Jpn. Kokai Tokkyo Koho, 4 pp. CODEN: JKXXAF, JP 57188503 A2 821119; Showa, Application Ser. No.: JP 81-74643 810518). Other chloromethyl oxadiazoles have been made and used to alkylate amines and other nucleophiles (Crovetti, A. J., et al., *J. Heterocycl.*

Chem., 9:435 (1972)). However, a systematic exploration of oxadiazoles has not been performed.

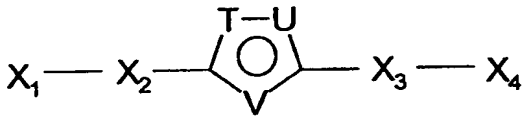
The general methods for the synthesis of 1,2,4-oxadiazoles fall into two categories: acylation and cyclization of amidoximes, or dipolar cycloaddition of nitrile oxides to nitriles (Lianis, P.S., et al., *J. Heterocyclic Chem.*, 26:1683 (1989)). The latter is possible only with highly activated nitriles and thus has limited utility. The most general method of synthesis relies on the acylation and cyclization of amidoximes. Amidoximes are prepared from aliphatic or aromatic nitriles by addition of hydroxylamine. Conversion to the oxadiazoles is realized by treatment with acid chlorides (Chiou, S., et al., *Chem. Ber.* 17:1685 (1984)) or anhydrides in refluxing pyridine (Claisse, J. A., et al. *J. Chem. Soc. Perkin I*, 2241 (1973)). Liang and Feng used the symmetrical anhydrides generated from 2-hydroxy carboxylic acids in the presence of a carbodiimide as the acylating species to give 5-hydroxymethyl substituted oxadiazoles (Liang, G. B., et al. *Tetrahedron Lett.*, 37: 6627 (1996)). However, in the majority of examples, only simple aliphatic or aromatic carboxylic acid derivatives have been used.

This invention satisfies these needs and provides related advantages as well. The present invention overcomes the known limitations to classical organic synthesis of oxadiazoles, for example, as well as the shortcomings of combinatorial chemistry related to heterocycles. The present invention allows for rapid generation of large diverse libraries of complex heterocycles as discrete molecules or molecules bound to a resin. The present invention can utilize a readily available pool of building blocks that can be incorporated into the various regions of the molecule.

Furthermore, the method of making the present invention allows for the use of building blocks that contain a wide range of diverse functionality. Therefore, building blocks, such as those described above, can provide libraries that consist of large numbers as well as libraries that are extremely diverse with respect to the functionality contained within those libraries. The present invention combines the techniques of solid-phase synthesis of heterocycles and the general techniques of synthesis of combinatorial libraries to prepare highly diverse new oxadiazole, thiadiazole and triazole compounds.

SUMMARY OF THE INVENTION

The present invention relates to novel oxadiazole, thiadiazole and triazole compounds of the following formula:



Formula (I)

wherein X_1, X_2, X_3, X_4, T, U and V have the meanings provided below.

The invention further relates to combinatorial libraries containing two or more such compounds, and to the generation of such combinatorial libraries composed of such compounds.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 provides Reaction Scheme 1 showing the attachment of cyanocarboxylic acids to solid support.

Figure 2 provides Reaction Scheme 2 showing the attachment of cyanophenols to solid support.

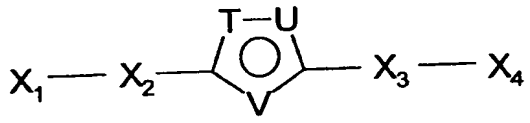
Figure 3 provides Reaction Scheme 3 showing linking nitriles to solid support.

Figure 4 provides Reaction Scheme 4 showing the conversion of resin-bound nitriles into oxadiazoles.

Figure 5 provides Reaction Scheme 5 showing the derivatization of oxadiazoles.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides novel compounds and libraries of novel compounds of Formula (I):



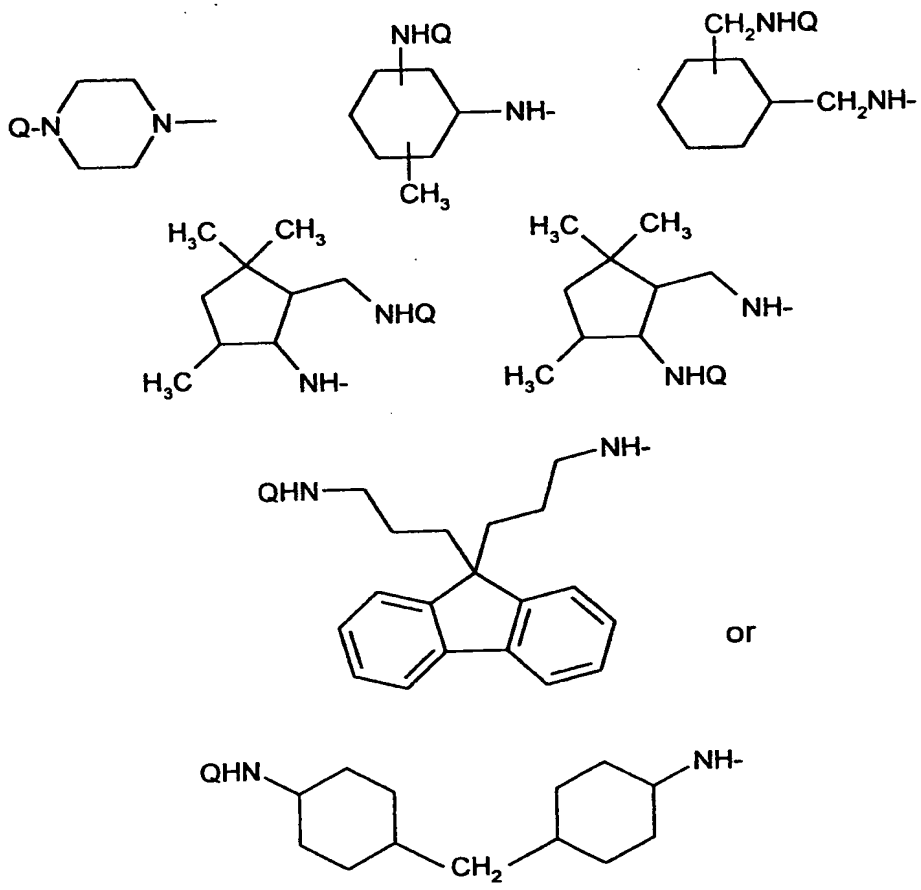
Formula (I)

wherein:

T, U and V are independently selected from an oxygen, sulfur or nitrogen atom, provided that at least two of T, U and V are a nitrogen atom;

X_1 is H, $-NHC(O)NR_1R_2$, $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$, or $-CH_2NR_1R_2$ wherein R_1 is a hydrogen atom or a functionalized resin; and R_2 is a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, phenyl,

substituted phenyl, naphthyl, substituted naphthyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, heteroaryl or substituted heteroaryl, heterocycle or substituted heterocycle; or $-NR_1R_2$ together is of the formula:



wherein Q is a hydrogen atom or functionalized resin; and

X_2 is C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_2 to C_7 alkenylene, C_2 to C_7 substituted alkenylene, C_2 to C_7 alkynylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, C_5 to C_7 cycloalkenylene, C_5 to C_7 substituted cycloalkenylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, or C_7 to C_{12} substituted phenylalkylene C_7 to C_{12} phenylalkox, or C_7 to C_{12} substituted phenylalkoxy; or

X_2 is of the formula:

$$-(CH_2)_m-G-(CH_2)_n-$$

wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and G is phenylene or substituted phenylene; or

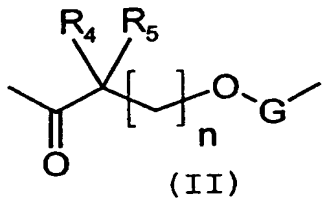
X_2 is of the formula:

$$-(CH_2)_m-NR_3-(CH_2)_n-$$

wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and R_3 is a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_4 alkyl sulfonyl, C_1 to C_4 substituted alkyl sulfonyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl; substituted phenylaminothiocarbonyl, C_1 to C_7

alkoxycarbonyl, C_1 to C_7 substituted alkoxycarbonyl, phenoxycarbonyl or substituted phenoxycarbonyl; or

X_2 is of the formula (II):

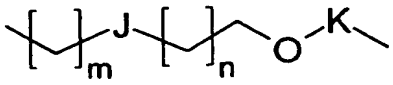


(II)

wherein n is an integer selected from 0 to 6; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl or protected hydroxymethyl; and

G is phenylene or substituted phenylene; or

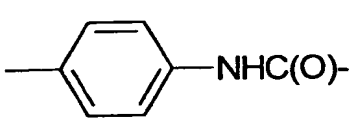
X_2 is of the formula (III):



(III)

wherein J is phenylene or substituted phenylene, K is phenylene or substituted phenylene, and m and n are independently selected from O and I; or

X_2 is of the formula (IV) or (V):



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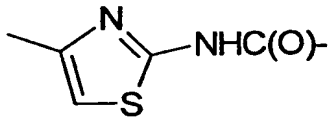
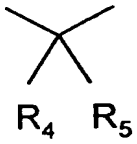


(V) ; and

X_3 is absent or of the formula:

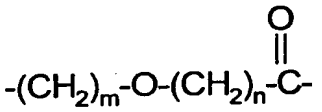


wherein:

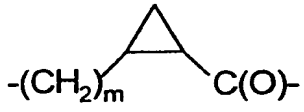
R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_1 to C_6 substituted alkyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring,

substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl or protected hydroxymethyl; or

X_3 is of the formula (VIa) or (VIb):



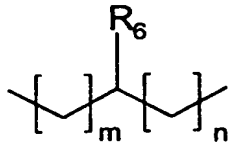
(VIa)



(VIb)

wherein in formula (VIa) m and n are independently selected from 0, 1, 2, 3 and 4 and, preferably, are 1; and wherein in formula (VIb) m is 0, 1, 2, 3 or 4 and, preferably, is 0; or

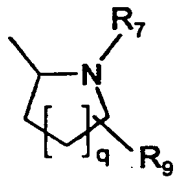
X_3 is of the formula:



wherein R_6 is a hydrogen atom, amino, amino-protecting group, $-NR_7R_8$, carboxy, carboxy-protecting group, $-C(O)NR_7R_8$ wherein R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12}

substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and m and n are independently selected from 0, 1, 2, 3 and 4; or

X_3 is of the formula (VII) to (XIII):



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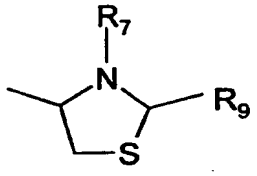

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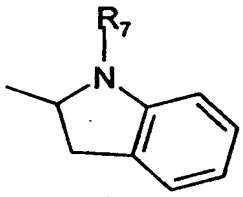

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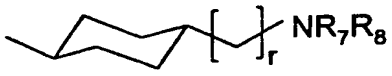
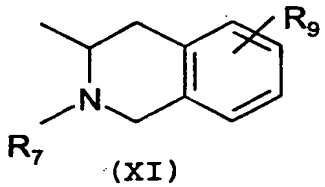


(X)



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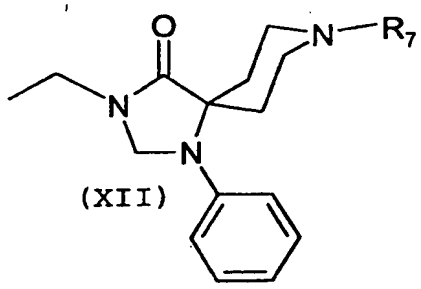

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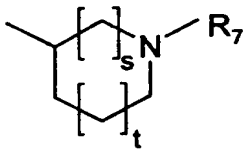


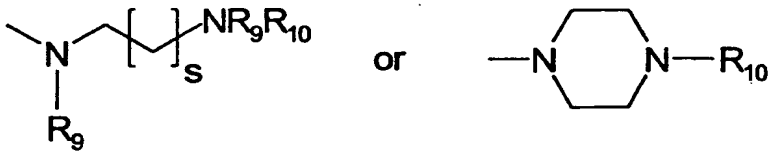
(XIII)

wherein q is 1 or 2; r is 0 or 1; s and t are independently selected from 0, 1 or 2; and

R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and

R_9 is a hydrogen atom, -OH, hydroxy-protecting group, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 phenylalkoxy, phenyl, substituted phenyl, heteroaryl or substituted heteroaryl; and

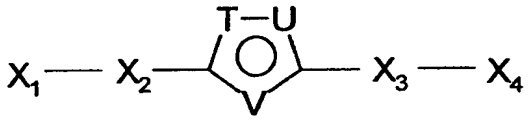
X_4 is absent or a hydrogen atom, -OH, $-CO_2H$, $-C(O)NR_7R_8$ or $-NR_7R_8$, wherein R_7 and R_8 are independently selected from a functionalized resin, a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; or $-NR_7R_8$ together is of the formula:



wherein R_9 and R_{10} are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and s is an integer selected from 1 to 5; or

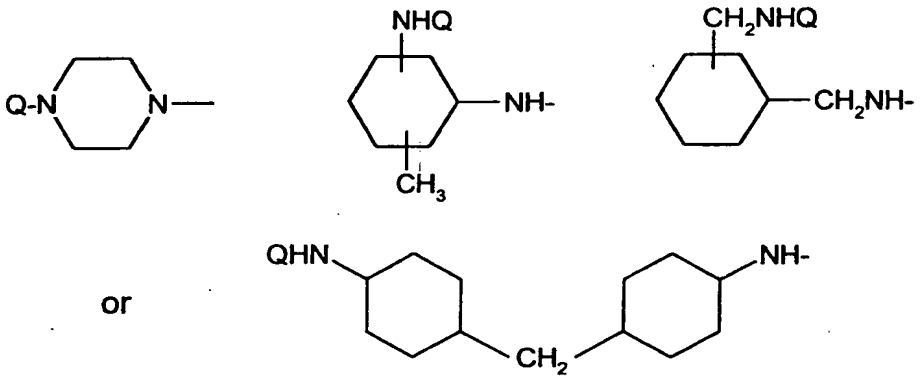
a pharmaceutically acceptable salt of a compound of the formula (I).

In a preferred embodiment of this invention, the oxadiazole compounds and libraries containing Formula (I):



Formula (I)

wherein T is N, U is O and V is N; and
X_1 is $-CO_2R_1$, $-OR_1$, $-NR_1R_2$ or $-C(O)NR_1R_2$; or $-NR_1R_2$ together is of the formula:



where Q is defined above; and

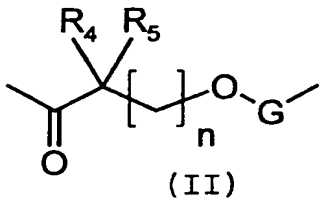
X_2 is C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, or C_7 to C_{12} substituted phenylalkylene; or

X_2 is of the formula:

$$-(CH_2)_m-NR_3-(CH_2)_n-$$

wherein m is 1 to 3 and n is 1 to 4; or

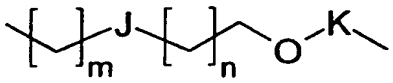
X_2 is of the formula (II):



(II)

wherein n is 0 or 1; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl or C_1 to C_{10} substituted alkyl; or

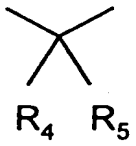
X_2 is of the formula (III):



(III)

wherein m and n are integers independently selected from 0 and 1; or

X_3 is absent or of the formula:

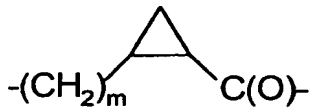


wherein:

R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl, C_7 to C_{12} substituted phenylalkyl, substituted phenyl, hydroxymethyl, protected

hydroxymethyl, C_3 to C_7 cycloalkyl or C_3 to C_7 substituted cycloalkyl; or

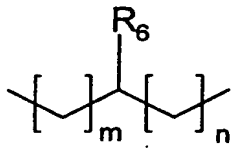
X_3 is of the formula (VIb):



(VIb)

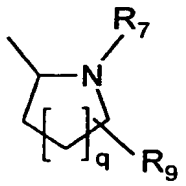
wherein m is 0; or

X_3 is of the formula:

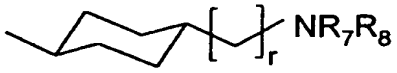


wherein m is 0 to 2 and n is 1 to 4, and R_6 is as described above; and

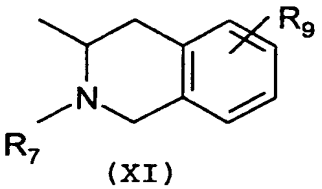
where X_3 is absent, X_4 is of the formula (VII), (X), (XI), (XII) or (XIII):



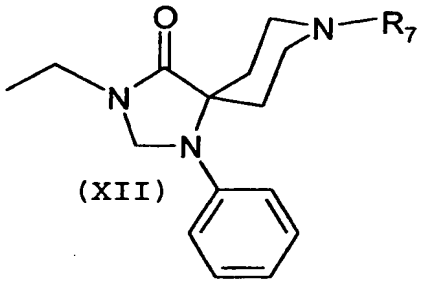
(VII)



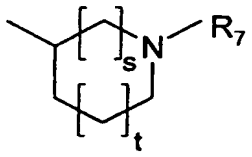
(X)



(XI)



(XII)

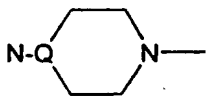


(XIII)

wherein R_9 is a hydrogen atom or -OH, and R_7, R_8, q, r, s and t are as described above.

In another preferred embodiment of this invention, the compounds and libraries are of Formula (I) wherein:

X_1 is $-CO_2R_1$, $-OR_1$, $-NR_1R_2$ or $-C(O)NR_1R_2$; or $-NR_1R_2$ together is of the formula:



where Q is defined above.

In another preferred embodiment of this invention, the compounds and libraries are of Formula (I) wherein:

U is oxygen, T is nitrogen and V is nitrogen;

X_1 is OH or $CONH_2$; or

X_1 is
2-(1-pyrrolidino)ethylamine,
2-pyridinemethylamine, 2-(4-imidazole)ethylamine,
cyclopentylamine, allylamine, 2-methoxyethylamine,
(+/-)-tetrahydrofurylamine, benzylamine,
2-methylbenzylamine, 3-methylbenzylamine,
4-methylbenzylamine, 2-fluorobenzylamine,
3-fluorobenzylamine, 4-fluorobenzylamine,
3-(1-imidazole)propylamine, 4-aminomethylbenzylamine,
4-methoxybenzylamine, 3-chlorobenzylamine,
3-bromobenzylamine, 4-bromobenzylamine,
cyclopropylamine, cyclopropanemethylamine,
4-pyridinemethylamine, 3-pyridinemethylamine,
2-thiophenemethylamine, phenethylamine,
2-(morpholine)ethylamine, 3- methoxybenzylamine,
piperonylamine, 4-methoxyphenethylamine,
2-fluorophenethylamine, 2-(4-chlorophenyl)ethylamine,
2-(3-chlorophenyl)ethylamine,
2-(2-chlorophenyl)ethylamine, 2,3-dimethoxy-
benzylamine, 3,4-dimethoxyphenethylamine, 2,4-
dichlorophenethylamine, 2-(diethylamino)ethylamine,
2-(1-methylpyrrolidin-2-yl)ethylamine,
3-(diethylamino)propylamine,
2-(5-nitro-2-pyridyl)ethylamine,
3-(dimethylamino)-2,2-dimethylpropylamine,
3-(dimethylamino)propylamine, 2-aminoethylamine,
2-(piperidino)ethylamine, isoamylamine,
3-ethoxypropylamine, 3-(2-pipecolinyl)propylamine,
3-butoxypropylamine,

3-(pyrrolidin-2-one-1-yl)propylamine,
3-(morpholino)propylamine,
2-(N-ethyl-3-methylanilino)ethylamine, 3-phenyl-1-propylamine, 2-methyl-2-phenylethylamine,
4-phenylbutylamine, 3,3-diphenylpropylamine,
isobutylamine, 2-(2-pyridyl)ethylamine,
cyclohexanemethylamine, 3-methoxyphenethylamine,
3-phenylbenzylamine, piperazine; and

X_2 is methylene, 1,1-cyclopropyl, 1,3-phenylene,
1,4-phenylene, 1-methyl-1-(4-oxyphenylene)ethane;
3-methoxy-1,4-phenylene, 2-fluoro-1,4-phenylene,
4,4'-biphenylene, 1,2-phenylene,
3,5-dibromo-1,4-phenylene, 4-phenyl-1-(methylene-1-yl),
3,5-diiodo-1,4-phenylene, 3-hydroxy-1,4-phenylene,
2,3,5,6-tetrafluoro-1,4-phenylene,
3-bromo-1,4-phenylene, 3,5-di-tert- butyl-1,4-phenylene,
3,5-di-tert-butyl-4-phenyl-1-(methylene-1-yl),
3-methoxy-4-phenyl-1-(methylene-1-yl),
3-nitro-1,4-phenylene, 5-hydroxy-1,3-phenylene,
4-phenyl-1-(-2-ethyl),
3-ethoxy-4-phenyl-1-(methylene-1-yl),
2-chloro-1,4-phenylene, 2-fluoro-1,4-phenylene,
3,5-dimethyl-1,4-phenylene, 2,6-dimethyl-1,4-phenylene,
3,5-dichloro-1,4-phenylene,
3-methoxy-2-phenyl-1-(methylene-1-yl), 8-quinoline-2-yl,
5-indole-3-(methylene-1-yl),
3,hydroxy-4-phenyl-1-(methylene-1-yl),
4-chloro-1,2-phenylene, 6-nitro-1,2-phenylene,
5-nitro-1,2-phenylene,
2-amino-1,4-phenylene,2-carboxymethyl-1,4-phenylene,
3-bromo-5-methoxy-4-phenyl-1-(methylene-1-yl),
3,5-dimethoxy-4-phenyl-1-(methylene-1-yl),
2-iodo-6-nitro-1,4-phenylene;

X_3 is 1-aminomethylene, 1-(1-aminoethyl),

1-(2-aminoethyl), 1-(1-amino-2-(3-pyridyl)ethyl), 1-(1-amino-2-(2-thienyl)ethyl), 1-(1-aminopropyl), 1-(3-aminopropyl), 1-(5-aminopentyl), 1-(1-methyl-1-aminoethyl), 1-(4-aminomethylcyclohexyl), 1-(1-amino-3-guanidinopropyl), 3-(3-aminopropionic acid), 3-(2-aminopropionic acid), 3-methylene-1-phenyl-1,3,8-triazaspiro[4.5]decane-4-one, 1-(1-amino-2-(4-chlorophenyl)ethyl), 1-(1-amino-2-(cyclohexyl)ethyl), 4-(4-aminobutyric acid),-4-(2-aminobutyric acid), -1-(1-amino-2-(4-imidazolyl)ethyl), -1-(1-amino-2-methylbutyl), -4-piperidinyl, 1-(1-amino-3-methylbutyl), 3-piperidinyl, 1-(1-aminobutyl), 1-(1-amino-2-phenylethyl), 2-piperidinyl, 2-pyrrolidinyl, 1-(1-amino-2-hydroxyethyl), 4-thiazolidinyl, 1-(1-amino-2-hydroxypropyl), 3-tetrahydroisoquinolinyl, 1-(1-amino-2-(3-indolyl)ethyl), 1-(1-amino-2-(4-hydroxyphenyl)ethyl), 1-(1-amino-2-(4-ethoxyphenyl)ethyl), 1-(1-amino-2-methylpropyl), 1-(1,5-diaminopentyl); or

X_3 is 2-(1-pyrrolidino)ethylaminomethylene, 2-pyridinemethylaminomethylene, 2-(4-imidazole)ethylaminomethylene, cyclopentylaminomethylene, allylaminomethylene, 2-methoxyethylaminomethylene, (+/-)-tetrahydrofurylaminomethylene, benzylaminomethylene, 2-methylbenzylaminomethylene, 3-methylbenzylaminomethylene, 4-methylbenzylaminomethylene, 2-fluorobenzylaminomethylene, 3-fluorobenzylaminomethylene, 4-fluorobenzylaminomethylene, 3-(1-imidazole)propylaminomethylene, 4-aminomethylbenzylaminomethylene, 4-methoxybenzylaminomethylene,

3-chlorobenzylaminomethylene,
3-bromobenzylaminomethylene,
4-bromobenzylaminomethylene, cyclopropylaminomethylene,
cyclopropanemethylaminomethylene,
4-pyridinemethylaminomethylene,
3-pyridinemethylaminomethylene,
2-thiophenemethylaminomethylene,
phenethylaminomethylene,
2-(morpholine)ethylaminomethylene, 3-
methoxybenzylaminomethylene, piperonylaminomethylene,
4-methoxyphenethylaminomethylene,
2-fluorophenethylaminomethylene,
2-(4-chlorophenyl)ethylaminomethylene,
2-(3-chlorophenyl)ethylaminomethylene,
2-(2-chlorophenyl)ethylaminomethylene, 2,3-dimethoxy-
benzylaminomethylene,
3,4-dimethoxyphenethylaminomethylene, 2,4-
dichlorophenethylaminomethylene,
2-(diethylamino)ethylaminomethylene,
2-(1-methylpyrrolidin-2-yl)ethylaminomethylene,
3-(diethylamino)propylaminomethylene,
2-(5-nitro-2-pyridyl)ethylaminomethylene,
3-(dimethylamino)-2,2-dimethylpropylaminomethylene,
3-(dimethylamino)propylaminomethylene,
2-aminoethylaminomethylene,
2-(piperidino)ethylaminomethylene,
isoamylaminomethylene, 3-ethoxypropylaminomethylene,
3-(2-pipecolinyl)propylaminomethylene,
3-butoxypropylaminomethylene,
3-(pyrrolidin-2-one-1-yl)propylaminomethylene,
3-(morpholino)propylaminomethylene,
2-(N-ethyl-3-methylanilino)ethylaminomethylene,
3-phenyl-1- propylaminomethylene,
2-methyl-2-phenylethylaminomethylene,
4-phenylbutylaminomethylene,
3,3-diphenylpropylaminomethylene,
isobutylaminomethylene,

2-(2-pyridyl)ethylaminomethylene,
cyclohexanemethylaminomethylene,
3-methoxyphenethylaminomethylene,
3-phenylbenzylaminomethylene, piperazinomethylene; and

X_4 is acetyl, alpha-methylcinnamyl, benzoyl, crotonyl, cyclobutanecarbonyl, cyclohexanepropionyl, 4-cyanobenzoyl, hydrocinnamyl, 4-dimethylaminobenzoyl, 4-ethoxybenzoyl, isobutyryl, 4- ethoxyphenylacetyl, isovaleryl, levulinyl, m-anisyl, m-toluyl, methoxyacetyl, isonicotinyl, p-tolylacetyl, picolinyl, piperonylyl, 4-fluoro-alpha- methylphenylacetyl, 4-fluorophenylacetyl, tetrahydro-3-furoyl, trans-3-(3-pyridyl)acrylyl, trimethylacetyl, triphenylacetyl, nicotinyl, (3,4-dimethoxyphenyl)acetyl, boc-isonipecotyl, (alpha-alpha-alpha-trifluoro-m-tolyl)acetyl, (methylthio)acetyl, (phenylthio)acetyl, 1-(4-chlorophenyl)-1- cyclopentanecarbonyl, 1-adamantaneacetyl, 1-naphthylacetyl, 1-phenyl-1-cyclopropanecarbonyl, 4-iodobenzoyl, 4-isopropoxybenzoyl, 2,4-dichlorobenzoyl, 4-methyl-1-cyclohexanecarbonyl, pyrrole-2- carbonyl, 4-methylvaleryl, 1-naphthylacetyl, 2-fluorobenzoyl, 1,3-phenylene diacetyl, 2-norbornaneacetyl, 2-pyrazinecarbonyl, 2-pyridylacetyl, 2-thiopheneacetyl, 3,4,5- triethoxybenzoyl, 3,4-methylenedioxyphenylacetyl, 3,4-dichlorobenzoyl, 4- isopropylbenzoyl, 3,4-dichlorophenylacetyl, 4-tert-butyl-cyclohexanecarbonyl, 4-sulfonamidobenzoyl, 3,5,5-trimethylhexanoyl, 3,5-bis(trifluoromethyl)-benzoyl, 5-bromo-2-chlorobenzoyl, 5-bromonicotinyl, 6-chloronicotinyl, 3,5-dimethyl-p-anisyl, 3-bromo-4-methylbenzoyl, 3,4,5- trimethoxyphenylacetyl, 3-benzoylpropionyl, 3,5-dichlorobenzoyl, 3-cyanobenzoyl, 3-fluoro-4-methylbenzoyl, 1-isoquinolinecarbonyl,

3-methyl-2-thiophenecarbonyl, 3-phenoxybenzoyl,
3-thiopheneacetyl, 4-biphenylacetyl,
4-bromophenylacetyl, s-(+)-mandelyl,
3,5-di-tert-butyl-4-hydroxybenzoyl,
3,5-dichloro-4-hydroxybenzoyl, 4- hydroxybenzoyl,
5-methylsalicylyl, 2-methylcyclopropanecarbonyl,
3-lndolepropionyl, 2,2-diphenylacetyl,
5-methoxyindole-2-carbonyl, succinamyl,
4-dimethylaminobutyryl, 4- methylthiobenzoyl,
2-methylthionicotinyl,
r(-)-2-oxothiazolidine-4-carbonyl, 4-nitrophenylacetyl,
coumarin-3-carbonyl, 1-cyano-1-cyclopropane carbonyl,
2-chloro-5-(methylthio)benzoyl, theophylline-7-acetyl,
2-(2-cyanophenylthio)benzoyl; or

X_4 is 2-mesitylenesulfonyl, 2-naphthalenesulfonyl,
2-thiophenesulfonyl, 4-chlorobenzenesulfonyl,
4-fluorobenzenesulfonyl, 4-methoxybenzenesulfonyl,
4-methylsulfonylbenzenesulfonyl, benzenesulfonyl,
dansyl, n-acetylsulfanilyl,
2-acetamido-4-methyl-5-thiazolesulfonyl,
4-(trifluoromethoxy)benzenesulfonyl,
4-tert-butylbenzenesulfonyl, 8-quinolinesulfonyl,
2,3-dichlorothiophene-5-sulfonyl,
3,4-dimethoxybenzenesulfonyl,
3,5-bis(trifluoromethyl)benzenesulfonyl,
3-chloro-4-fluorobenzenesulfonyl,
3-trifluoromethylbenzenesulfonyl,
4-ethylbenzenesulfonyl, pentamethylbenzenesulfonyl,
2,3,4-trifluorobenzenesulfonyl,
2,4-dichlorobenzenesulfonyl,
2,5-dichlorothiophene-3-sulfonyl,
2,6-dichlorobenzenesulfonyl,
2,6-difluorobenzenesulfonyl,
2-chloro-4-(trifluoromethyl)benzenesulfonyl,
2-chloro-5-(trifluoromethyl)benzenesulfonyl,

2-chloro-6-methylbenzenesulfonyl,
3,4-difluorobenzenesulphonyl,
3,5-dichlorobenzenesulfonyl, 3-chlorobenzenesulfonyl,
4-(n-butoxy)benzenesulfonyl, 4-trifluoromethylbenzene sulfonyl, 3,5- dimethylisoxazole-4-sulfonyl,
2-(methoxycarbonyl)thiophene-3-sulfonyl,
4-acetamido-3-chlorobenzene sulfonyl,
2-[1-methyl-5-(trifluoromethyl)pyrazol-3-yl]thiophene-5-sulfonyl, 2-(benzoylaminomethyl)thiophene-5-sulfonyl,
3-methoxy-4-(methoxycarbonyl)-thiophene-2-sulfonyl,
5-(isoxazol-3-yl)thiophene-2-sulfonyl, 4-cyanobenzene sulfonyl, 3-chloro-4-methylbenzenesulfonyl,
2,4-difluorobenzenesulfonyl, 2-fluorobenzenesulfonyl,
4-isopropylbenzene sulfonyl,
2,5-dimethoxybenzenesulfonyl,
3,4-dichlorobenzenesulfonyl; or

X_4 is (2s,3s)-2-(carbamyl)-3-methylvalerate methyl ester,
(r)-(-)-1-(carbamyl)-(1-naphthyl)ethane,
(s)-(+)-1-(carbamyl)-(1-naphthyl)ethane,
(s)-(+)-2-(carbamyl)-3-tert-butoxypropionate methyl ester, (s)-(-)-2-(carbamyl)-3-methylbutyrate methyl ester, (s)-(-)-2-(carbamyl)-4-(methylthio)butyrate methyl ester, (s)-(-)-2-(carbamyl)-4-methylvalerate methyl ester, (s)-(-)-2-(carbamyl)glutarate diethyl ester, (s)-(-)-2-(carbamyl)propionate methyl ester,
(s)-2-(carbamyl)-3- phenylpropionate methyl ester,
1-(carbamyl)-tridecafluoro-1-hexane,
1-(carbamyl)-1,1,3,3-tetramethylbutane,
1-(carbamyl)-(1-naphthyl)ethane,
1-(carbamyl)-(4-bromophenyl)ethane,
1-(carbamyl)-adamantane, 1-(carbamyl)naphthalene,
1-(carbamyl)-2,3,4-trifluorobenzene,
1-(carbamyl)-2,3-dichlorobenzene,
1-(carbamyl)-2,3-dimethylbenzene,
1-(carbamyl)-2,4,5-trichlorobenzene,
1-(carbamyl)-2,4,5-trimethylbenzene,

1-(carbamyl)-2,4,6-trichlorobenzene,
1-(carbamyl)-2,4-dichlorobenzene, 1-(carbamyl)-2,4-difluorobenzene, 1-(carbamyl)-2,4-dimethoxybenzene,
1-(carbamyl)-2,4-dimethylbenzene,
1-(carbamyl)-2,5-dichlorobenzene,
1-(carbamyl)-2,5-difluorobenzene,
1-(carbamyl)-2,5-dimethoxybenzene,
1-(carbamyl)-2,5- dimethylbenzene,
1-(carbamyl)-2,6-dibromo-4-fluorobenzene,
1-(carbamyl)-2,6-dibromo-4-isopropylbenzene,
1-(carbamyl)-2,6-dichlorobenzene,
1-(carbamyl)-2,6-diethylbenzene,
1-(carbamyl)-2,6-difluorobenzoyl,
1-(carbamyl)-2,6-difluorobenzene,
1-(carbamyl)-2,6-diisopropylbenzene,
1-(carbamyl)-2,6-dimethylbenzene,
1-(carbamyl)-2-(chloromethyl)benzene,
1-(carbamyl)-2-(difluoromethoxy)benzene,
1-(carbamyl)-2-(methylthio)benzene,
1-(carbamyl)-2-(trifluoromethoxy)benzene,
1-(carbamyl)-2-(trifluoromethyl)benzene,
1-(carbamyl)-2-biphenyl,
1-(carbamyl)-2-bromo-4,6-difluorobenzene,
1-(carbamyl)-2-bromoethane, 1-(carbamyl)-2-bromobenzene,
1-(carbamyl)-2-chloro-4-nitrobenzene,
1-(carbamyl)-2-chloro-5-(trifluoromethyl)benzene,
1-(carbamyl)-2-chloro-5-nitrobenzene,
1-(carbamyl)-2-chloro-6-methylbenzene,
1-(carbamyl)-2-chlorobenzyl,
1-(carbamyl)-2-chloroethane,
1-(carbamyl)-2-chlorobenzene,
1-(carbamyl)-2-cyanobenzene,
1-(carbamyl)-2-ethoxybenzene,
1-(carbamyl)-2-ethyl-6-methylbenzene,
1-(carbamyl)-2-ethylbenzene,
1-(carbamyl)-2-fluoro-3-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluoro-5-(trifluoromethyl)benzene,

1-(carbamyl)-2-fluoro-5-methylbenzene,
1-(carbamyl)-2-fluoro-5-nitrobenzene,
1-(carbamyl)-2-fluoro-6-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluorobenzene,
1-(carbamyl)-2-iodobenzene,
1-(carbamyl)-2-isopropyl-6-methylbenzene,
1-(carbamyl)-2-isopropylbenzene,
1-(carbamyl)-2-methoxy-5-chloro benzene,
1-(carbamyl)-2-methoxy-5-methylbenzene,
1-(carbamyl)-2-methoxy-5-nitrobenzene,
1-(carbamyl)-2-methoxybenzene,
1-(carbamyl)-2-methyl-3-nitrobenzene,
1-(carbamyl)-2-methyl-5-nitrobenzene,
1-(carbamyl)-2-methyl-6-t-butylbenzene,
1-(carbamyl)-1-(2-methylphenyl)methane,
1-(carbamyl)-2-n-propylbenzene,
1-(carbamyl)-2-naphthalene, 1-(carbamyl)-2-nitrobenzene,
1-(carbamyl)-2-phenoxybenzene,
1-(carbamyl)-2-tert-butylbenzene,
1-(carbamyl)-3,4,5-trimethoxybenzene,
1-(carbamyl)-1-(3,4-dichlorophenyl)methane,
1-(carbamyl)-3,4-dichlorobenzene,
1-(carbamyl)-3,4-difluorobenzene,
1-(carbamyl)-3,4-dimethylbenzene,
1-(carbamyl)-3,5-bis(trifluoromethyl)benzene,
1-(carbamyl)-3,5- dichlorobenzene,
1-(carbamyl)-3,5-dimethoxybenzene,
1-(carbamyl)-3,5-dimethylbenzene, 1-(carbamyl)-3,5-dinitrobenzene, 1-(carbamyl)-3-(methylthio)benzene,
1-(carbamyl)-3-(trifluoromethyl)benzene,
1-(carbamyl)-3-(trifluoromethylthio)benzene,
1-(carbamyl)-3-acetylbenzene,
1-(carbamyl)-3-bromobenzene,
1-(carbamyl)-3-bromopropane,
1-(carbamyl)-3-carbomethoxybenzene,
1-(carbamyl)-3-chloro-2-methoxybenzene,
1-(carbamyl)-3-chloro-2-methylbenzene,

1-(carbamyl)-3-chloro-4-fluorobenzene,
1-(carbamyl)-3-chloro-4-methylbenzene,
1-(carbamyl)-3-chlorobenzene,
1-(carbamyl)-3-chloropropane,
1-(carbamyl)-3-cyanobenzene,
1-(carbamyl)-3-cyclopentoxy-4-methoxybenzene,
1-(carbamyl)-3-ethylbenzene,
1-(carbamyl)-3-fluoro-4-methylbenzene,
1-(carbamyl)-3-fluorobenzene,
1-(carbamyl)-3-iodopropane, 3-(carbamyl)benzoyl chloride, 1-(carbamyl)-3-methoxybenzene,
1-(carbamyl)-(3-methylphenyl)methane,
1-(carbamyl)-3-nitrobenzene, 1-(carbamyl)-3-pyridine,
4'-(carbamyl)-5'-nitrobenzo-15-crown-5,
4'-(carbamyl)benzo-15-crown-5,
4'-(carbamyl)benzo-18-crown-6,
1-(carbamyl)-4,5-dimethyl-2-nitrobenzene,
1-(carbamyl)-4-(6-methyl-2-benzothiazolyl)benzene,
1-(carbamyl)-4-(chloromethyl)benzene,
1-(carbamyl)-4-(chlorosulfonyl)benzene,
1-(carbamyl)-4-(difluoromethoxy)benzene,
1-(carbamyl)-4-(methylthio)benzene,
1-(carbamyl)-4-(tert-butyl)benzene,
1-(carbamyl)-4-(trifluoromethoxy)benzene,
1-(carbamyl)-4-(trifluoromethyl)benzene,
1-(carbamyl)-4-(trifluoromethylthio)benzene,
1-(carbamyl)-4-acetylbenzene,
1-(carbamyl)-4-benzyloxybenzene,
1-(carbamyl)-4-bromo-2,6-dimethylbenzene,
1-(carbamyl)-4-bromo-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-bromo-2-chlorobenzene,
1-(carbamyl)-4-bromo-2-fluorobenzene,
1-(carbamyl)-4-bromo-2-methylbenzene,
1-(carbamyl)-4-bromobenzene,
1-(carbamyl)-4-chloro-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-chloro-2-methoxybenzene,
1-(carbamyl)-4-chloro-2-methylbenzene,

1-(carbamyl)-4-chloro-2-nitrobenzene,
1-(carbamyl)-4-chloro-3-(trifluoromethyl)benzene,
1-(carbamyl)-4-chloro-3-nitrobenzene,
1-(carbamyl)-4-chlorobenzene,
1-(carbamyl)-4-dimethylaminobenzene,
1-(carbamyl)-4-ethoxybenzene,
1-(carbamyl)-4-ethylbenzene,
1-(carbamyl)-4-fluoro-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-fluoro-2-nitrobenzene,
1-(carbamyl)-4-fluoro-3-(trifluoromethyl)benzene,
1-(carbamyl)-4-fluoro-3-nitrobenzene,
1-(carbamyl)-4-fluorobenzoyl,
1-(carbamyl)-4-fluorobenzyl,
1-(carbamyl)-4-fluorobenzene,
1-(carbamyl)-4-heptyloxybenzene,
1-(carbamyl)-4-iodobenzene, 4-(carbamyl)benzoyl chloride, 1-(carbamyl)-4-isopropylbenzene,
1-(carbamyl)-4-methoxy-2-methylbenzene,
1-(carbamyl)-(4-methoxyphenyl)methane,
1-(carbamyl)-4-methoxybenzene,
1-(carbamyl)-4-methyl-2-nitrobenzene,
1-(carbamyl)-4-methyl-3-nitrobenzene,
1-(carbamyl)-(4-methylphenyl)methane,
1-(carbamyl)-4-n-butoxycarbonylbenzene,
1-(carbamyl)-4-n-butoxybenzene,
1-(carbamyl)-4-n-butyl-2-methylbenzene,
1-(carbamyl)-4-n-butylbenzene,
1-(carbamyl)-4-nitrobenzene,
1-(carbamyl)-4-phenoxybenzene,
1-(carbamyl)-5-bromopenane,
1-(carbamyl)-5-chloro-2,4-dimethoxybenzene,
1-(carbamyl)-5-chloro-2-methylbenzene,
1-(carbamyl)-5-fluoro-2-methylbenzene,
1-(carbamyl)-5-iodopentane, 1-(carbamyl)-2-propene, benzoyl carbamyl, 1-(carbamyl)-1-phenylmethane,
1-(carbamyl)-cyclohexane, carboxyethylcarbamyl, ethyl 2-(carbamyl)-3-methylbutyrate, ethyl

2-(carbamyl)-3-phenylpropionate, ethyl 2-(carbamyl)-4-(methylthio)butyrate, ethyl 2-(carbamyl)-4-methylvalerate, ethyl 2-(carbamyl)benzoate, ethyl 2-(carbamyl)propionate, ethyl 3-(carbamyl)benzoate, ethyl 3-(carbamyl)propionate, ethyl 4-(carbamyl)-benzoate, ethyl 6-(carbamyl)hexanoate, 1-(carbamyl)-ethyl, ethyl (carbamyl)acetate, 1-(carbamyl)-heptane, 1-(carbamyl)-hexane, 1-(carbamyl)-2-methylpropane, 1-(carbamyl)ethyl methacrylate, 1-(carbamyl)-2-methylethane, methyl 2-(carbamyl)benzoate, carbamylmethane, methyl(carbamyl)propionate, 1-(carbamyl)butane, n-butyl (carbamyl)acetate, 1-(carbamyl)-propane, 1-(carbamyl)-pentane, 1-(carbamyl)-phenylthane, 1-(carbamyl)-benzene, 1-(carbamyl)-2,2-dimethylpropane, 1-(carbamyl)-tetrahydro-2-pyran, 1-(carbamyl)-trans-2-benzenecyclopropane, 1-(carbamyl)-trichloroacetate, carbamyltrichloromethane; or

X_4 is 1-(thiocarbamyl)-(2-methoxy-5-phenyl)benzene, 1-(thiocarbamyl)adamantane, 1-(thiocarbamyl)naphthalenemethane, (thiocarbamyl)naphthalene, 1-(thiocarbamyl)2,2-diphenylethane, 1-(thiocarbamyl)-2,3,4,5-tetrachlorobenzene, 1-(thiocarbamyl)-2,3,4-trichlorobenzene, 1-(thiocarbamyl)-(2,3,4-trimethoxyphenyl)methane, 1-(thiocarbamyl)-2,3,5,6-tetrachlorobenzene, 1-(thiocarbamyl)-2,3,5,6-tetrafluorobenzene, 1-(thiocarbamyl)-2,3-dibromopropane, 1-(thiocarbamyl)-2,3-dichlorobenzene, 1-(thiocarbamyl)-(2,3-dimethoxyphenyl)methane, 1-(thiocarbamyl)-2,3-dimethylbenzene, 1-(thiocarbamyl)-2,4,5-trichlorobenzene, 1-(thiocarbamyl)-2,4,6-tribromobenzene,

1-(thiocarbamyl)-2,4,6-trichlorobenzene,
1-(thiocarbamyl)-2,4,6-trifluorobenzene,
1-(thiocarbamyl)-2,4,6-trimethylbenzene,
1-(thiocarbamyl)-2,4-dichlorobenzene,
1-(thiocarbamyl)-2,4-difluorobenzene,
1-(thiocarbamyl)-2,4-dimethoxybenzene,
1-(thiocarbamyl)-2,4-dimethylbenzene,
1-(thiocarbamyl)-2,5-dibromobenzene,
1-(thiocarbamyl)-2,5-dichlorobenzene,
1-(thiocarbamyl)-2,5-difluorobenzene,
1-(thiocarbamyl)-2,5-dimethoxybenzene,
1-(thiocarbamyl)-2,5-dimethylbenzene,
1-(thiocarbamyl)-2,6-dichlorobenzene,
1-(thiocarbamyl)-2,6-diethylbenzene,
1-(thiocarbamyl)-2,6-difluorobenzene,
1-(thiocarbamyl)-2,6-diisopropylbenzene,
1-(thiocarbamyl)-2,6-dimethylbenzene,
1-(thiocarbamyl)-2-(3,4-dimethoxyphenyl)ethane,
1-(thiocarbamyl)-2-(4-chlorophenyl)ethane,
1-(thiocarbamyl)-2-(methylthio)benzene,
1-(thiocarbamyl)-2-(trifluoromethoxy)benzene,
1-(thiocarbamyl)-2-(trifluoromethyl)benzene,
1-(thiocarbamyl)-2-bromo-4-methylbenzene,
1-(thiocarbamyl)-2-bromoethane,
1-(thiocarbamyl)-2-bromobenzene,
1-(thiocarbamyl)-2-chloro-4-methylbenzene,
1-(thiocarbamyl)-2-chloro-4-nitrobenzene,
1-(thiocarbamyl)-2-chloro-5-(trifluoromethyl)benzene,
1-(thiocarbamyl)-2-chloro-5-nitrobenzene,
1-(thiocarbamyl)-2-chloro-6-methylbenzene,
1-(thiocarbamyl)-(2-chlorophenyl)methane,
1-(thiocarbamyl)-2-chloroethane,
1-(thiocarbamyl)-2-chlorobenzene,
1-(thiocarbamyl)-2-cyanobenzene,
1-(thiocarbamyl)-2-ethoxycarbonylbenzene,
1-(thiocarbamyl)-2-ethoxybenzene,
1-(thiocarbamyl)-2-ethyl-6-(1-methylpropyl)benzene,

1-(thiocarbamyl)-2-ethyl-6-isopropylbenzene,
1-(thiocarbamyl)-2-ethyl-6-methylbenzene,
1-(thiocarbamyl)-2-ethylbenzene,
1-(thiocarbamyl)-(2-fluorophenyl)methane,
1-(thiocarbamyl)-2-fluoroethane,
1-(thiocarbamyl)-2-fluorobenzene, 2-(thiocarbamyl)furan,
2-(thiocarbamyl)hexane, 1-(thiocarbamyl)-2-iodobenzene,
1-(thiocarbamyl)-2-isopropyl-6-methylbenzene,
1-(thiocarbamyl)-2-isopropylbenzene,
1-(thiocarbamyl)-2-methoxy-4-nitrobenzene,
1-(thiocarbamyl)-2-methoxy-5-methylbenzene,
1-(thiocarbamyl)-2-methoxy-5-nitrobenzene,
1-(thiocarbamyl)-(2-methoxyphenyl)methane,
1-(thiocarbamyl)-2-methoxyethane,
1-(thiocarbamyl)-2-methoxybenzene,
1-(thiocarbamyl)-2-methyl-4-nitrobenzene,
1-(thiocarbamyl)-2-methyl-5-nitrobenzene,
1-(thiocarbamyl)-(2-methylphenyl)methane,
1-(thiocarbamyl)-2-methylbutane,
1-(thiocarbamyl)-2-(morpholino)ethane,
2-(thiocarbamyl)-naphthalene, 2-(thiocarbamyl)pentane,
1-(thiocarbamyl)-2-phenylethane,
1-(thiocarbamyl)-2-piperidinoethane,
2-(thiocarbamylmethyl)-tetrahydrofuran,
1-(thiocarbamyl)-3,4,5-trimethoxybenzene,
1-(thiocarbamyl)-3,4-(ethylenedioxy)benzene,
1-(thiocarbamyl)-3,4-dichlorophenyl)methane,
1-(thiocarbamyl)-3,4-dichlorobenzene,
1-(thiocarbamyl)-(3,4-dimethoxyphenyl)methane,
1-(thiocarbamyl)-3,4-dimethoxybenzene,
1-(thiocarbamyl)-3,4-dimethylbenzene,
1-(thiocarbamyl)-(3,4-methylenedioxyphenyl)methane,
1-(thiocarbamyl)-3,4-methylenedioxybenzene,
1-(thiocarbamyl)-3,5-bis(trifluoromethyl)benzene,
1-(thiocarbamyl)-3,5-dichlorobenzene,
1-(thiocarbamyl)-3,5-dimethoxybenzene,
1-(thiocarbamyl)-3,5-dimethylbenzene,

1-(thiocarbamyl)-3-(diethylamino)propane,
1-(thiocarbamyl)-3-(methylthio)benzene,
1-(thiocarbamyl)-3-(trifluoromethyl)benzene,
1-(thiocarbamyl)-3-acetylbenzene,
1-(thiocarbamyl)-3-benzyloxybenzene,
1-(thiocarbamyl)-3-bromobenzene,
1-(thiocarbamyl)-3-bromopropane,
1-(thiocarbamyl)-3-carboxybenzene,
1-(thiocarbamyl)-3-chloro-2-methylbenzene,
1-(thiocarbamyl)-3-chloro-4-fluorobenzene,
1-(thiocarbamyl)-(3-chloro-4-methylphenyl)methane,
1-(thiocarbamyl)-3-chloro-4-methylbenzene,
1-(thiocarbamyl)-(3-chlorophenyl)methane,
1-(thiocarbamyl)-3-chlorobenzene,
1-(thiocarbamyl)-3-chloropropane,
1-(thiocarbamyl)-3-cyanobenzene,
1-(thiocarbamyl)-3-dimethylaminopropane,
1-(thiocarbamyl)-3-ethoxycarbonylbenzene,
1-(thiocarbamyl)-3-ethylbenzene,
1-(thiocarbamyl)-(3-fluorophenyl)methane,
1-(thiocarbamyl)-3-fluorobenzene,
1-(thiocarbamyl)-3-iodobenzene,
1-(thiocarbamyl)-(3-methoxyphenyl)methane,
1-(thiocarbamyl)-3-methoxycarbonylbenzene,
1-(thiocarbamyl)-3-methoxybenzene,
1-(thiocarbamyl)-3-methoxypropane,
1-(thiocarbamyl)-3-methyl-2-butane,
1-(thiocarbamyl)-(3-methylphenyl)methane,
1-(thiocarbamyl)-3-methylbutane,
1-(thiocarbamyl)-3-morpholinopropane,
1-(thiocarbamyl)-3-nitrobenzene,
1-(thiocarbamyl)-3-pentane,
1-(thiocarbamyl)-3-phenylpropane,
3-(thiocarbamyl)pyridine,
1-(thiocarbamyl)-4-(benzyloxy)benzene,
1-(thiocarbamyl)-4-(dimethylamino)benzene,
1-(thiocarbamyl)-4-(methylthio)benzene,

1-(thiocarbamyl)-4-(trifluoromethoxy)benzene,
1-(thiocarbamyl)-4-(trifluoromethyl)benzene,
1-(thiocarbamyl)-4-acetylbenzene,
1-(thiocarbamyl)-4-bromo-2,6-dimethylbenzene,
1-(thiocarbamyl)-4-bromo-2-chlorobenzene,
1-(thiocarbamyl)-4-bromo-2-methylbenzene,
1-(thiocarbamyl)-4-bromo-2-trifluoromethylbenzene,
1-(thiocarbamyl)-4-bromobenzene,
1-(thiocarbamyl)-4-carboxybenzene,
1-(thiocarbamyl)-4-chloro-2-(trifluoromethyl)benzene,
1-(thiocarbamyl)-4-chloro-2-methylbenzene,
1-(thiocarbamyl)-4-chloro-3-nitrobenzene,
1-(thiocarbamyl)-4-chloro-3-trifluoromethylbenzene,
1-(thiocarbamyl)-(4-chlorophenyl)methane,
1-(thiocarbamyl)-4-chlorobenzene,
1-(thiocarbamyl)-4-cyanobenzene,
1-(thiocarbamyl)-4-diethylaminobenzene,
1-(thiocarbamyl)-4-ethoxycarbonylbenzene,
1-(thiocarbamyl)-4-ethoxybenzene,
1-(thiocarbamyl)-4-ethylbenzene,
1-(thiocarbamyl)-4-fluoro-2-methylbenzene,
1-(thiocarbamyl)-(4-fluorophenyl)ethane,
1-(thiocarbamyl)-(4-fluorophenyl)methane,
1-(thiocarbamyl)-4-fluorobenzene,
1-(thiocarbamyl)-4-iodobenzene,
1-(thiocarbamyl)-4-isopropylbenzene,
1-(thiocarbamyl)-4-methoxy-2-methylbenzene,
1-(thiocarbamyl)-4-methoxy-2-nitrobenzene,
1-(thiocarbamyl)-(4-methoxyphenyl)methane,
1-(thiocarbamyl)-4-methoxycarbonylbenzene,
1-(thiocarbamyl)-4-methoxybenzene,
1-(thiocarbamyl)-4-methyl-2-nitrobenzene,
1-(thiocarbamyl)-(4-methylphenyl)methane,
1-(thiocarbamyl)-4-n-butyl-2-methylbenzene,
1-(thiocarbamyl)-4-n-butylbenzene,
1-(thiocarbamyl)-4-nitrobenzene,
1-(thiocarbamyl)-4-phenoxybenzene,

1-(thiocarbamyl)-4-phenylazobenzene,
1-(thiocarbamyl)-4-phenylbutane,
1-(thiocarbamyl)-4-sulfamoylbenzene,
1-(thiocarbamyl)-4-tert-butylbenzene,
1-(thiocarbamyl)-5-chloro-2,4-dimethoxybenzene,
1-(thiocarbamyl)-5-chloro-2-methoxybenzene,
1-(thiocarbamyl)-5-chloro-2-methylbenzene,
1-(thiocarbamyl)-5-fluoro-2-methylbenzene,
1-(thiocarbamyl)-5-indane,
2-(thiocarbamyl)-5-norbornene,
2-(thiocarbamyl)-6-methylheptane,
9-(thiocarbamyl)acridine, 1-(thiocarbamyl)-2-propene,
1-(thiocarbamyl)-(1-phenyl)ethane,
1-(thiocarbamyl)-phenylmethane,
1-(thiocarbamyl)-cycloheptane,
1-(thiocarbamyl)-cyclohexylmethane,
1-(thiocarbamyl)-cyclohexane,
1-(thiocarbamyl)-cyclooctane,
1-(thiocarbamyl)-cyclopentane,
1-(thiocarbamyl)-cyclopropane, diethyl
L-2-thiocarbamyl-glutarate, dimethyl
L-thiocarbamyl-succinate, ethyl
2-thiocarbamylpropionate, ethyl 3-thiocarbamylbutyrate,
ethyl 3-thiocarbamylpropionate, ethyl
4-thiocarbamylbutyrate, 1-(thiocarbamyl)-ethane, ethyl
thiocarbamylacetate, 1-(thiocarbamyl)-2-methylpropane,
1-(thiocarbamyl)-1-methylethane,
thiocarbamylacetaldehyde dimethyl acetal,
thiocarbamylphenyl sulfone, 1-(thiocarbamyl)-2-butene,
1-(thiocarbamyl)-methoxymethane, methyl
2-thiocarbamylacetate, methyl 2-thiocarbamylbenzoate,
methyl 3-thiocarbamylpropionate, methyl
2-thiocarbamylbutyrate, methyl, methyl
L-2-thiocarbamyl-3-methyl-butyrate, methyl
L-2-thiocarbamyl-3-phenyl-propionate, methyl
L-2-thiocarbamyl-4-(methylthio)butyrate, methyl
L-2-thiocarbamyl-4-methylvalerate,

1-(thiocarbamyl)-pentane, 1-(thiocarbamyl)-butane,
1-(thiocarbamyl)-hexane, 1-(thiocarbamyl)-propane,
2-(thiocarbamyl)-norbornane,
1-(thiocarbamyl)-4-vinylbenzene,
1-(thiocarbamyl)-pentafluorobenzene,
1-(thiocarbamyl)-benzene, 1-(thiocarbamyl)-propyne,
2-(thiocarbamyl)-butane.

The present invention also provides a method of preparing libraries wherein compounds of Formula (I), in particular, oxadiazoles, are made by reacting a resin-bound amine with a nitrile-containing carboxylic acid, nitrile-containing isocyanate or nitrile-containing radical with a leaving group to obtain a resin-bound nitrile; cyclizing the nitrile to obtain an oxadiazole containing an amino-protected group; deprotecting the amino-protected group to obtain an oxadiazole amine; and reacting the oxadiazole amine with a carboxylic acid or a sulfonyl chloride or an isocyanate or an isothiocyanate to obtain the oxadiazole library. Another method of preparing oxadiazole libraries comprises reacting a resin-bound amine with a nitrile-containing carboxylic acid, isocyanate or leaving group to obtain a resin-bound nitrile; cyclizing the nitrile to obtain an oxadiazole containing a leaving group; and reacting the leaving group with a primary amine or secondary amine to obtain a oxadiazole secondary amine or oxadiazole tertiary amine; and optionally reacting the secondary amine with a carboxylic acid or a sulfonyl chloride or an isocyanate or an isothiocyanate to obtain the oxadizaole library. In a preferred embodiment the resin-bound amine can be prepared by displacing a resin-bound leaving group with a primary amine. In another embodiment, the resin-bound amine can be prepared by reducing a resin-bound imine formed from either a resin-bound aldehyde with a primary amine or a resin-bound primary amine with an aldehyde.

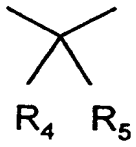
Yet another method comprises reacting a resin-bound leaving group with a nitrile-containing phenoxide ion or amine to obtain a resin-bound nitrile; cyclizing the nitrile to obtain to an oxadiazole containing an amino-protected group; deprotecting the amino-protected group to obtain an amine; and reacting the amine with a carboxylic acid or a sulfonyl chloride or an isocyanate or an isothiocyanate to obtain the oxadiazole library. Still another method comprises reacting a resin-bound leaving group with a nitrile-containing phenoxide ion to obtain a resin-bound nitrile; cyclizing the nitrile to obtain an oxadiazole containing a leaving group; and reacting the leaving group with a primary or secondary amine to obtain a secondary or a tertiary amine of the oxadiazole library; and optionally reacting the secondary amine with a carboxylic acid or a sulfonyl chloride or an isocyanate or an isothiocyanate to obtain the oxadizaole library.

Alternatively, the present invention also provides a method of preparing oxadiazole libraries wherein oxadiazole compounds of Formula (I) are made by reducing an imine formed between a resin-bound aldehyde and an amine containing a protected carboxylic acid to give a protected carboxylic acid bound to resin; deprotecting the protected carboxylic acid to give a resin bound carboxylic acid and reacting the carboxylic acid with an amidoxime to give an oxadiazole library.

Another method of preparing oxadiazole libraries comprises reacting a resin-bound alcohol with an amine containing a protected carboxylic acid to give a protected carboxylic acid bound to resin through a carbamate linkage; deprotecting the protected carboxylic acid to give a carboxylic acid and reacting the carboxylic acid with an amidoxime to give an oxadiazole library.

In a preferred embodiment, the methods described above further comprise the step of cleaving the library from the resin.

In the above Formula (I), the stereochemistry of chiral centers associated with R_2 and R_3 when X_3 is:



can independently be in the R or S configuration, or a mixture of the two. The chiral centers can be further designated as R or S or R,S or d,D, l,L or d,l, D,L.

In the above Formula (I), the term "C_1 to C_6 alkyl" denotes such radicals as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, amyl, tert-amyl, hexyl and the like. The preferred "C_1 to C_6 alkyl" groups are methyl, iso-butyl, sec-butyl and iso-propyl.

The term "C_2 to C_7 alkenyl" denotes such radicals as vinyl, allyl, 2-butenyl, 3-butenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, 2-hexenyl, 3-hexenyl, 4-hexenyl, 5-hexenyl, 2-heptenyl, 3-heptenyl, 4-heptenyl, 5-heptenyl, 6-heptenyl, as well as dienes and trienes of straight and branched chains.

The term "C_2 to C_7 alkynyl" denotes such radicals as ethynyl, propynyl, 2-butynyl, 2-pentynyl, 3-pentynyl, 2- hexynyl, 3-hexynyl, 4-hexynyl, 2-heptynyl, 3-heptynyl, 4- heptynyl, 5-heptynyl as well as di- and tri-ynes of straight and branched chains.

The terms "C_1 to C_6 substituted alkyl," "C_2 to C_7 substituted alkenyl," "C_2 to C_7 substituted alkynyl," and "C_1 to C_{12} substituted alkylene" denote that the above C_1 to C_6 alkyl groups and C_2 to C_7 alkenyl and C_2 to C_7 alkynyl groups and C_1 to C_{12} alkylene are substituted by one or more, and preferably one or two, halogen, hydroxy, protected hydroxy, oxo, protected oxo, C_3 to C_7 cycloalkyl, naphthyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N,N-di(C_1 to C_6 alkyl)carboxamide, cyano, methylsulfonylamino, thiol, C_1 to C_4 alkylthio or C_1 to C_4 alkylsulfonyl groups. The substituted alkyl groups may be substituted once or more, and preferably once or twice, with the same or with different substituents.

Examples of the above substituted alkyl groups include the 2-oxo-prop-1-yl, 3-oxo-but-1-yl, cyanomethyl, nitromethyl, chloromethyl, hydroxymethyl, tetrahydropyranyloxymethyl, trityloxymethyl, propionyloxymethyl, amino, methylamino, aminomethyl, dimethylamino, carboxymethyl, allyloxycarbonylmethyl, allyloxycarbonylaminomethyl, methoxymethyl, ethoxymethyl, t-butoxymethyl, acetoxymethyl, chloromethyl, bromomethyl, iodomethyl, trifluoromethyl, 6-hydroxyhexyl, 2,4-dichloro(n-butyl), 2-aminopropyl, 1-chloroethyl, 2-chloroethyl, 1- bromoethyl, 2-chloroethyl, 1-fluoroethyl, 2-fluoroethyl, 1- iodoethyl, 2-iodoethyl, 1-chloropropyl, 2-chloropropyl, 3- chloropropyl, 1-bromopropyl, 2-bromopropyl, 3-bromopropyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, 1- iodopropyl, 2-

iodopropyl, 3-iodopropyl, 2-aminoethyl, 1- aminoethyl, N-benzoyl-2-aminoethyl, N-acetyl-2-aminoethyl, N-benzoyl-1-aminoethyl, N-acetyl-1-aminoethyl and the like.

Examples of the above substituted alkenyl groups include styrenyl, 3-chloro-propen-1-yl, 3-chloro-buten-1-yl, 3-methoxy-propen-2-yl, 3-phenyl-buten-2-yl, 1-cyano-buten-3-yl and the like. The geometrical isomerism is not critical, and all geometrical isomers for a given substituted alkenyl can be used.

Examples of the above substituted alkynyl groups include phenylacetylen-1-yl, 1-phenyl-2-propyn-1-yl and the like.

The term "C_2 to C_7 alkenylene" as used herein denotes an alkene group that is linked by two different substitutents. Similarly, the term "C_2 to C_7 alkynylene" as used herein denotes an alkyne group that is linked by two different substitutents. The term "C_2 to C_7 substituted alkenylene" as used herein denotes an alkene group that is linked by two different substitutents and is further substituted by one or two halogen, hydroxy, protected hydroxy, oxo, protected oxo, C_3 to C_7 cycloalkyl, naphthyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N,N-di(C_1 to C_6 alkyl)carboxamide, cyano, methylsulfonylamino, thiol, C_1 to C_4 alkylthio or C_1 to C_4 alkylsulfonyl groups.

The term "oxo" denotes a carbon atom bonded to two additional carbon atoms substituted with an oxygen atom doubly bonded to the carbon atom, thereby forming a ketone moiety.

The term "protected oxo" denotes a carbon atom bonded to two additional carbon atoms substituted with two alkoxy groups or twice bonded to a substituted diol moiety, thereby forming an acyclic or cyclic ketal moiety.

The term "C_1 to C_7 alkoxy" as used herein denotes groups such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, t-butoxy and like groups. A preferred alkoxy is methoxy. The term "C_1 to C_7 substituted alkoxy" means the alkyl portion of the alkoxy can be substituted in the same manner as in relation to C_1 to C_6 substituted alkyl. Similalry, the term "C_1 to C_7 phenylalkoxy" as used herein means "C_1 to C_7 alkoxy" bonded to a phenyl raidcal.

The term "C_1 to C_7 acyloxy" denotes herein groups such as formyloxy, acetoxy, propionyloxy, butyryloxy, pivaloyloxy, pentanoyloxy, hexanoyloxy, heptanoyloxy and the like.

Similarly, the term "C_1 to C_7 acyl" encompasses groups such as formyl, acetyl, propionyl, butyryl, pentanoyl, pivaloyl, hexanoyl, heptanoyl, benzoyl and the like. Preferred acyl groups are acetyl and benzoyl.

The term "C_1 to C_7 substituted acyl" denotes the acyl group substituted by one or more, and preferably one or two, halogen, hydroxy, protected hydroxy, oxo, protected oxo, cyclohexyl, naphthyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino,

heterocyclic ring, substituted heterocyclic ring, imidazolyl, indolyl, pyrrolidinyl, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, nitro, C_1 to C_6 alkyl ester, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N,N-di(C_1 to C_6 alkyl)carboxamide, cyano, methylsulfonylamino, thiol, C_1 to C_4 alkylthio or C_1 to C_4 alkylsulfonyl groups. The substituted acyl groups may be substituted once or more, and preferably once or twice, with the same or with different substituents.

Examples of C_1 to C_7 substituted acyl groups include 4-phenylbutyroyl, 3-phenylbutyroyl, 3-phenylpropanoyl, 2- cyclohexanylacetyl, cyclohexanecarbonyl, 2-furanoyl and 3-dimethylaminobenzoyl.

The substituent term "C_3 to C_7 cycloalkyl" includes the cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl rings. The substituent term "C_3 to C_7 substituted cycloalkyl" indicates the above cycloalkyl rings substituted by one or two halogen, hydroxy, protected hydroxy, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfoxide, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylthio, C_1 to C_4 substituted alkylsulfoxide, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, oxo, protected oxo, (monosubstituted)amino, (disubstituted)amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, or protected amino groups.

The term "C_3 to C_7 cycloalkylene" means a cycloalkyl, as defined above, where the cycloalkyl radical is bonded at two positions connecting together

two separate additional groups. Similarly, the term "C_3 to C_7 substituted cycloalkylene" means a cycloalkylene where the cycloalkyl radical is bonded at two positions connecting together two separate additional groups and further bearing at least one additional substituent.

The term "C_5 to C_7 cycloalkenyl" indicates a 1,2, or 3- cyclopentenyl ring, a 1,2,3 or 4-cyclohexenyl ring or a 1,2,3,4 or 5-cycloheptenyl ring, while the term "substituted C_5 to C_7 cycloalkenyl" denotes the above C_5 to C_7 cycloalkenyl rings substituted by a C_1 to C_6 alkyl radical, halogen, hydroxy, protected hydroxy, C_1 to C_7 alkoxy, trifluoromethyl, carboxy, protected carboxy, oxo, protected oxo, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, phenyl, substituted phenyl, amino, or protected amino.

The term "C_5 to C_7 cycloalkenylene" is a cycloalkenyl ring, as defined above, where the cycloalkenyl radical is bonded at two positions connecting together two separate additional groups. Similarly, the term "substituted C_5 to C_7 cycloalkenylene" means a cycloalkeneylene further substituted by halogen, hydroxy, protected hydroxy, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfoxide, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylthio, C_1 to C_4 substituted alkylsulfoxide, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, oxo, protected oxo, (monosubstituted)amino, (disubstituted)amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, or protected amino group.

The term "heterocycle" or "heterocyclic ring" denotes optionally substituted five-membered or six-membered rings that have 1 to 4 heteroatoms, such as

oxygen, sulfur and/or nitrogen, in particular nitrogen, either alone or in conjunction with sulfur or oxygen ring atoms. These five-membered or six-membered rings may be saturated, fully saturated or partially unsaturated, with fully saturated rings being preferred. An "amino-substituted heterocyclic ring" means any one of the above-described heterocyclic rings is substituted with at least one amino group. Preferred heterocyclic rings include morpholino, piperidinyl, piperazinyl, tetrahydrofurano, pyrrolo, and tetrahydrothiophen-yl.

The term "substituted heterocyce" or "substituted heterocyclic ring" means the above-described heterocyclic ring is substituted with, for example, one or more, and preferably one or two, substituents which are the same or different which substituents can be halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino or N-(phenylsulfonyl)amino groups.

The term "heteroaryl" means a heterocyclic aromatic derivative which is a five-membered or six-membered ring system having from 1 to 4 heteroatoms, such as oxygen, sulfur and/or nitrogen, in particular nitrogen, either alone or in conjunction with sulfur or oxygen ring atoms. Examples of heteroaryls include pyridinyl, pyrimidinyl, and pyrazinyl, pyridazinyl, pyrrolo, furano, oxazolo, isoxazolo, phthalimido, thiazolo and the like.

The term "substituted heteroaryl" means the above-described heteroaryl is substituted with, for example, one or more, and preferably one or two, substituents which are the same or different which substituents can be halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino or N-(phenylsulfonyl)amino groups.

The term "C_7 to C_{12} phenylalkyl" denotes a C_1 to C_6 alkyl group substituted at any position by a phenyl, substituted phenyl, heteroaryl or substituted heteroaryl. Examples of such a group include benzyl, 2-phenylethyl, 3-phenyl(n-propyl), 4-phenylhexyl, 3-phenyl(n-amyl), 3-phenyl(sec-butyl) and the like. Preferred C_7 to C_{12} phenylalkyl groups are the benzyl and the phenylethyl groups.

The term "C_7 to C_{12} substituted phenylalkyl" denotes a C_7 to C_{12} phenylalkyl group substituted on the C_1 to C_6 alkyl portion with one or more, and preferably one or two, groups chosen from halogen, hydroxy, protected hydroxy, oxo, protected oxo, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino, protected guanidino, heterocyclic ring, substituted heterocyclic ring, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_7 acyloxy, nitro, carboxy, protected carboxy,

carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-(C_1 to C_6 dialkyl)carboxamide, cyano, N-(C_1 to C_6 alkylsulfonyl)amino, thiol, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfonyl groups; and/or the phenyl group may be substituted with one or more, and preferably one or two, substituents chosen from halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl) carboxamide, protected N-(C_1 to C_6 alkyl) carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino, cyclic C_2 to C_7 alkylene or a phenyl group, substituted or unsubstituted, for a resulting biphenyl group. The substituted alkyl or phenyl groups may be substituted with one or more, and preferably one or two, substituents which can be the same or different.

Examples of the term "C_7 to C_{12} substituted phenylalkyl" include groups such as 2-phenyl-1-chloroethyl, 2-(4-methoxyphenyl)ethyl, 4-(2,6-dihydroxy phenyl)n-hexyl, 2-(5-cyano-3-methoxyphenyl)n-pentyl, 3-(2,6-dimethylphenyl)n-propyl, 4-chloro-3-aminobenzyl, 6-(4-methoxyphenyl)-3-carboxy(n-hexyl), 5-(4-aminomethylphenyl)- 3-(aminomethyl)n-pentyl, 5-phenyl-3-oxo-n-pent-1-yl and the like.

The term "C_7 to C_{12} phenylalkylene" specifies a C_7 to C_{12} phenylalkyl, as defined above, where the phenylalkyl radical is bonded at two positions connecting

together two separate additional groups. The definition includes groups of the formula: -phenyl-alkyl- and -alkyl-phenyl-alkyl- where "-" represents a bond. Substitutions on the phenyl ring can be 1,2, 1,3 or 1,4. The term "C_7 to C_{12} substituted phenylalkylene" means a C_7 to C_{12} phenylalkylene as defined above that is further substituted by halogen, hydroxy, protected hydroxy, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfoxide, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylthio, C_1 to C_4 substituted alkylsulfoxide, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, oxo, protected oxo, (monosubstituted)amino, (disubstituted)amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, or protected amino group on the phenyl ring or on the alkyl group.

The term "substituted phenyl" specifies a phenyl group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino or phenyl, wherein the phenyl is substituted or unsubstituted, such that, for example, a biphenyl results.

Examples of the term "substituted phenyl" includes a mono- or di(halo)phenyl group such as 2, 3 or 4-chlorophenyl, 2,6-dichlorophenyl, 2,5-dichlorophenyl, 3,4-dichlorophenyl, 2, 3 or 4-bromophenyl, 3,4-dibromophenyl, 3-chloro-4-fluorophenyl, 2, 3 or 4-fluorophenyl and the like; a mono or di(hydroxy)phenyl group such as 2, 3 or 4-hydroxyphenyl, 2,4-dihydroxyphenyl, the protected-hydroxy derivatives thereof and the like; a nitrophenyl group such as 2, 3 or 4-nitrophenyl; a cyanophenyl group, for example, 2, 3 or 4-cyanophenyl; a mono- or di(alkyl)phenyl group such as 2, 3 or 4-methylphenyl, 2,4-dimethylphenyl, 2, 3 or 4-(iso-propyl)phenyl, 2, 3 or 4-ethylphenyl, 2, 3 or 4-(n-propyl)phenyl and the like; a mono or di(alkoxyl)phenyl group, for example, 2,6-dimethoxyphenyl, 2, 3 or 4-methoxyphenyl, 2, 3 or 4-ethoxyphenyl, 2, 3 or 4-(isopropoxy)phenyl, 2, 3 or 4-(t-butoxy)phenyl, 3-ethoxy-4-methoxyphenyl and the like; 2, 3 or 4-trifluoromethylphenyl; a mono- or dicarboxyphenyl or (protected carboxy)phenyl group such as 2, 3 or 4-carboxyphenyl or 2,4-di(protected carboxy)phenyl; a mono-or di(hydroxymethyl)phenyl or (protected hydroxymethyl)phenyl such as 2, 3, or 4-(protected hydroxymethyl)phenyl or 3,4-di(hydroxymethyl)phenyl; a mono- or di(aminomethyl)phenyl or (protected aminomethyl)phenyl such as 2, 3 or 4-(aminomethyl)phenyl or 2,4-(protected aminomethyl)phenyl; or a mono- or di(N-(methylsulfonylamino))phenyl such as 2, 3 or 4-(N-(methylsulfonylamino))phenyl. Also, the term "substituted phenyl" represents disubstituted phenyl groups wherein the substituents are different, for example, 3-methyl-4-hydroxyphenyl, 3-chloro-4-hydroxyphenyl, 2-methoxy-4-bromophenyl, 4-ethyl-2-hydroxyphenyl, 3-hydroxy-4-nitrophenyl, 2-hydroxy 4-chlorophenyl and the like.

The term "phenoxy" denotes a phenyl bonded to an oxygen atom. The term "substituted phenoxy" specifies a phenoxy group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino and N-(phenylsulfonyl)amino.

Examples of substituted phenoxy include 2-methylphenoxy, 2-ethylphenoxy, 2-propylphenoxy, 2-isopropylphenoxy, 2-sec-butylphenoxy, 2-tert-butylphenoxy, 2-allylphenoxy, 2-propenylphenoxy, 2-cyclopentylphenoxy, 2-fluorophenoxy, 2-(trifluoromethyl)phenoxy, 2-chlorophenoxy, 2-bromophenoxy, 2-methoxyphenoxy, 2-ethoxyphenoxy, 2-isopropoxyphenoxy, 3-methylphenoxy, 3-ethylphenoxy, 3-isopropylphenoxy, 3-tert-butylphenoxy, 3-pentadecylphenoxy, 3-(trifluoromethyl)phenoxy, 3-fluorophenoxy, 3-chlorophenoxy, 3-bromophenoxy, 3-iodophenoxy, 3-methoxyphenoxy, 3-(trifluoromethoxy)phenoxy, 4-methylphenoxy, 4-ethylphenoxy, 4-propylphenoxy, 4-isopropylphenoxy, 4-sec-butylphenoxy, 4-tert-butylphenoxy, 4-tert-amylphenoxy, 4-nonylphenoxy, 4-dodecylphenoxy, 4-cyclopenylphenoxy, 4-(trifluoromethyl)phenoxy, 4-fluorophenoxy, 4-chlorophenoxy, 4-bromophenoxy, 4-iodophenoxy, 4-methoxyphenoxy, 4-(trifluoromethoxy)phenoxy, 4-ethoxyphenoxy,

4-propoxyphenoxy, 4-butoxyphenoxy, 4-hexyloxyphenoxy, 4-heptyloxyphenoxy, 2,3-dimethylphenoxy, 5,6,7,8-tetrahydro-1-naphthoxy, 2,3-dichlorophenoxy, 2,3-dihydro-2,2-dimethyl-7-benzofuranoxy, 2,3-dimethoxyphenoxy, 2,6-dimethylphenoxy, 2,6-diisopropylphenoxy, 2,6-di-sec-butylphenoxy, 2-tert-butyl-6-methylphenoxy, 2,6-di-tert-butylphenoxy, 2-allyl-6-methylphenoxy, 2,6-difluorophenoxy, 2,3-difluorophenoxy, 2,6-dichlorophenoxy, 2,6-dibromophenoxy, 2-fluoro-6-methoxyphenoxy, 2,6-dimethoxyphenoxy, 3,5-dimethylphenoxy, 5-isopropyl-3-methylphenoxy, 3,5-di-tert-butylphenoxy, 3,5-bis(trifluoromethyl)phenoxy, 3,5-difluorophenoxy, 3,5-dichlorophenoxy, 3,5-dimethoxyphenoxy, 3-chloro-5-methoxyphenoxy, 3,4-dimethylphenoxy, 5-indanoxy, 5,6,7,8-tetrahydro-2-naphthoxy, 4-chloro-3-methylphenoxy, 2,4-dimethylphenoxy, 2,5-dimethylphenoxy, 2-isopropyl-5-methylphenoxy, 4-isopropyl-3-methylphenoxy, 5-isopropyl-2-methylphenoxy, 2-tert-butyl-5-methylphenoxy, 2-tert-butyl-4-methylphenoxy, 2,4-di-tert-butylphenoxy, 2,4-di-tert-amylphenoxy, 4-fluoro-2-methylphenoxy, 4-fluoro-3-methylphenoxy, 2-chloro-4-methylphenoxy, 2-chloro-5-methylphenoxy, 4-chloro-2-methylphenoxy, 4-chloro-3-ethylphenoxy, 2-bromo-4-methylphenoxy, 4-iodo-2-methylphenoxy, 2-chloro-5-(trifluoromethyl)phenoxy, 2,4-difluorophenoxy, 2,5-difluorophenoxy, 3,4-difluorophenoxy, 4-chloro-2-fluorophenoxy, 3-chloro-4-fluorophenoxy, 4-chloro-3-fluorophenoxy, 2-bromo-4-fluorophenoxy, 4-bromo-2-fluorophenoxy, 2-bromo-5-fluorophenoxy, 2,4-dichlorophenoxy, 3,4-dichlorophenoxy, 2,5-dichlorophenoxy, 2-bromo-4-chlorophenoxy, 2-chloro-4-fluorophenoxy, 4-bromo-2-chlorophenoxy, 2,4-dibromophenoxy, 2-methoxy-4-methylphenoxy, 4-allyl-2-methylphenoxy, trans-2-ethoxy-5-(1-propenyl)phenoxy, 2-methoxy-4-propenylphenoxy, 3,4-dimethoxyphenoxy, 3-ethoxy-4-methoxyphenoxy, 4-allyl-2,6-dimethoxyphenoxy,

3,4-methylenedioxyphenoxy, 2,3,6-trimethylphenoxy, 2,4-dichloro-3-methylphenoxy, 2,3,4-trifluorophenoxy, 2,3,6-trifluorophenoxy, 2,3,5-trifluorophenoxy, 2,3,4-trichlorophenoxy, 2,3,6-trichlorophenoxy, 2,3,5-trimethylphenoxy, 3,4,5-trimethylphenoxy, 4-chloro-3,5-dimethylphenoxy, 4-bromo-3,5-dimethylphenoxy, 2,4,6-trimethylphenoxy, 2,6-bis(hydroxymethyl)-4-methylphenoxy, 2,6-di-tert-butyl-4-methylphenoxy, 2,6-di-tert-butyl-4-methoxyphenoxy, 2,4,5- trifluorophenoxy, 2-chloro-3,5-difluorophenoxy, 2,4,6-trichlorophenoxy, 3,4,5-trimethoxyphenoxy, 2,3,5-trichlorophenoxy, 4-bromo-2,6-dimethylphenoxy, 4-bromo-6-chloro-2-methylphenoxy, 2,6-dibromo-4-methylphenoxy, 2,6-dichloro-4-fluorophenoxy, 2,6-dibromo-4-fluorophenoxy, 2,4,6-tribromophenoxy, 2,4,6-triiodophenoxy, 2-chloro-4,5-dimethylphenoxy, 4-chloro-2-isopropyl-5-methylphenoxy, 2-bromo-4,5-difluorophenoxy, 2,4,5-trichlorophenoxy, 2,3,5,6-tetrafluorophenoxy and the like.

The term "C_7 to C_{12} substituted phenylalkoxy" denotes a C_7 to C_{12} phenylalkoxy group wherein the C_1 to C_6 alkyl portion is substituted with one or more, and preferably one or two, groups selected from halogen, hydroxy, protected hydroxy, oxo, protected oxo, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, guanidino, heterocyclic ring, substituted heterocyclic ring, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, nitro, carboxy, protected carboxy, carbamoyl, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N,N-(C_1 to C_6 dialkyl)carboxamide, cyano, N-(C_1 to C_6 alkylsulfonyl)amino, thiol, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfonyl groups; and/or the phenyl group can be substituted with one or more, and preferably one or two, substituents chosen from halogen, hydroxy, protected

hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl) carboxamide, protected N-(C_1 to C_6 alkyl) carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino, N-(phenylsulfonyl)amino or a phenyl group, substituted or unsubstituted, for a resulting biphenyl group. The substituted alkyl or phenyl groups may be substituted with one or more, and preferably one or two, substituents which can be the same or different.

Examples of the term "C_7 to C_{12} substituted phenylalkoxy" include groups such as 2-(4-hydroxyphenyl)ethoxy, 4-(4-methoxyphenyl)butoxy, (2R)-3-phenyl-2-amino-propoxy, (2S)-3-phenyl-2-amino-propoxy, 2-indanoxy, 6-phenyl-1-hexanoxy, cinnamyloxy, (+/-)-2-phenyl-1-propoxy, 2,2-dimethyl-3-phenyl-1-propoxy and the like.

The term "phthalimide" means a cyclic imide which is made from phthalic acid, also called 1,2-benzenedicarboxylic acid. The term "substituted phthalimide" specifies a phthalimide group substituted with one or more, and preferably one or two, moieties chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_7 substituted alkoxy, C1 to C_7 acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide,

N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino and N-(phenylsulfonyl)amino.

Examples of substituted phthalimides include 4,5-dichlorophthalimido, 3-fluorophthalimido, 4-methoxyphthalimido, 3-methylphthalimido, 4-carboxyphthalimido and the like.

The term "substituted naphthyl" specifies a naphthyl group substituted with one or more, and preferably one or two, moieties either on the same ring or on different rings chosen from the groups consisting of halogen, hydroxy, protected hydroxy, cyano, nitro, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_7 acyl, C_1 to C_7 acyloxy, carboxy, protected carboxy, carboxymethyl, protected carboxymethyl, hydroxymethyl, protected hydroxymethyl, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, carboxamide, protected carboxamide, N-(C_1 to C_6 alkyl)carboxamide, protected N-(C_1 to C_6 alkyl)carboxamide, N, N-di(C_1 to C_6 alkyl)carboxamide, trifluoromethyl, N-((C_1 to C_6 alkyl)sulfonyl)amino or N-(phenylsulfonyl)amino.

Examples of the term "substituted naphthyl" includes a mono or di(halo)naphthyl group such as 1, 2, 3, 4, 5, 6, 7 or 8-chloronaphthyl, 2, 6-dichloronaphthyl, 2, 5-dichloronaphthyl, 3, 4-dichloronaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-bromonaphthyl, 3, 4-dibromonaphthyl, 3-chloro-4-fluoronaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-fluoronaphthyl and the like; a mono or di(hydroxy)naphthyl group such as 1, 2, 3, 4, 5, 6, 7 or 8-hydroxynaphthyl, 2, 4-dihydroxynaphthyl, the protected-hydroxy derivatives thereof and the like; a nitronaphthyl group such as 3- or 4-nitronaphthyl; a cyanonaphthyl

group, for example, 1, 2, 3, 4, 5, 6, 7 or 8-cyanonaphthyl; a mono- or di(alkyl)naphthyl group such as 2, 3, 4, 5, 6, 7 or 8-methylnaphthyl, 1, 2, 4-dimethylnaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-(isopropyl)naphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-ethylnaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-(n-propyl)naphthyl and the like; a mono or di(alkoxy)naphthyl group, for example, 2, 6-dimethoxynaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-methoxynaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-ethoxynaphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-(isopropoxy)naphthyl, 1, 2, 3, 4, 5, 6, 7 or 8-(t-butoxy)naphthyl, 3-ethoxy-4-methoxynaphthyl and the like; 1, 2, 3, 4, 5, 6, 7 or 8-trifluoromethylnaphthyl; a mono- or dicarboxynaphthyl or (protected carboxy)naphthyl group such as 1, 2, 3, 4, 5, 6, 7 or 8-carboxynaphthyl or 2, 4-di(-protected carboxy)naphthyl; a mono-or di(hydroxymethyl)naphthyl or (protected hydroxymethyl)naphthyl such as 1, 2, 3, 4, 5, 6, 7 or 8-(protected hydroxymethyl)naphthyl or 3, 4-di(hydroxymethyl)naphthyl; a mono- or di(amino)naphthyl or (protected amino)naphthyl such as 1, 2, 3, 4, 5, 6, 7 or 8-(amino)naphthyl or 2, 4-(protected amino)-naphthyl, a mono- or di(aminomethyl)naphthyl or (protected aminomethyl)naphthyl such as 2, 3, or 4-(aminomethyl)naphthyl or 2, 4-(protected aminomethyl)-naphthyl; or a mono- or di-(N-methylsulfonylamino) naphthyl such as 1, 2, 3, 4, 5, 6, 7 or 8-(N-methylsulfonylamino)naphthyl. Also, the term "substituted naphthyl" represents disubstituted naphthyl groups wherein the substituents are different, for example, 3-methyl-4-hydroxynaphth-1-yl, 3-chloro-4-hydroxynaphth-2-yl, 2-methoxy-4-bromonaphth-1-yl, 4-ethyl-2-hydroxynaphth-1-yl, 3-hydroxy-4-nitronaphth-2-yl, 2-hydroxy-4-chloronaphth-1-yl, 2-methoxy-7-bromonaphth-1-yl, 4-ethyl-5-hydroxynaphth-2-yl,

3-hydroxy-8-nitronaphth-2-yl, 2-hydroxy-5-chloronaphth-1-yl and the like.

The term "naphthylene" means a naphthyl radical bonded at two positions connecting together two separate additional groups. Similarly, the term "substituted napthylene" means a naphthylene group that is further substituted by halogen, hydroxy, protected hydroxy, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfoxide, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylthio, C_1 to C_4 substituted alkylsulfoxide, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, oxo, protected oxo, (monosubstituted)amino, (disubstituted)amino, trifluoromethyl, carboxy, protected carboxy, phenyl, substituted phenyl, phenylthio, phenylsulfoxide, phenylsulfonyl, amino, or protected amino group.

The terms "halo" and "halogen" refer to the fluoro, chloro, bromo or iodo atoms. There can be one or more halogen, which are the same or different. Preferred halogens are chloro and fluoro.

The term "(monosubstituted)amino" refers to an amino group with one substituent chosen from the group consisting of phenyl, substituted phenyl, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 alkynyl, C_2 to C_7 substituted alkynyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl and heterocyclic ring. The (monosubstituted)amino can additionally have an amino-protecting group as encompassed by the term "protected (monosubstituted)amino."

The term "(disubstituted)amino" refers to an amino group with two substituents chosen from the group

consisting of phenyl, substituted phenyl, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_7 to C_{12} phenylalkyl, and C_7 to C_{12} substituted phenylalkyl. The two substituents can be the same or different.

The term "amino-protecting group" as used herein refers to substituents of the amino group commonly employed to block or protect the amino functionality while reacting other functional groups of the molecule. The term "protected (monosubstituted)amino" means there is an amino-protecting group on the monosubstituted amino nitrogen atom. In addition, the term "protected carboxamide" means there is an amino-protecting group on the carboxamide nitrogen. Similarly, the term "protected N-(C_1 to C_6 alkyl)carboxamide" means there is an amino-protecting group on the carboxamide nitrogen.

Examples of such amino-protecting groups include the formyl ("For") group, the trityl group, the phthalimido group, the trichloroacetyl group, the chloroacetyl, bromoacetyl, and iodoacetyl groups, urethane-type blocking groups, such as t-butoxycarbonyl ("Boc"), 2-(4-biphenylyl)propyl-2-oxycarbonyl ("Bpoc"), 2-phenylpropyl-2-oxycarbonyl ("Poc"), 2-(4-xenyl)isopropoxycarbonyl, 1,1-diphenylethyl-1-oxycarbonyl, 1,1-diphenylpropyl-1-oxycarbonyl, 2-(3,5-dimethoxyphenyl)propyl-2-oxycarbonyl ("Ddz"), 2-(p-toluyl)propyl-2-oxycarbonyl, cyclopentanyloxycarbonyl, 1-methylcyclopentanyloxycarbonyl, cyclohexanyloxy-carbonyl, 1-methylcyclohexanyloxycarbonyl, 2-methylcyclohexanyloxycarbonyl, 2-(4-toluylsulfonyl)-ethoxycarbonyl, 2-(methylsulfonyl)ethoxycarbonyl, 2-(triphenylphosphino)-ethoxycarbonyl, 9-fluorenylmethoxycarbonyl ("Fmoc"), 2-(trimethylsilyl)ethoxycarbonyl, allyloxycarbonyl, 1-(trimethylsilylmethyl)prop-1-enyloxycarbonyl,

5-benzisoxalylmethoxycarbonyl, 4-acetoxybenzyl-oxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2-ethynyl-2-propoxycarbonyl, cyclopropylmethoxycarbonyl, isobornyloxycarbonyl, 1-piperidyloxycarbonyl, benzyloxycarbonyl ("Cbz"), 4-phenylbenzyloxycarbonyl, 2-methylbenzyloxy-carbonyl, - 2,4,5,-tetramethylbenzyloxycarbonyl ("Tmz"), 4-methoxybenzyloxycarbonyl, 4-fluorobenzyloxycarbonyl, 4-chlorobenzyloxycarbonyl, 3-chlorobenzyloxycarbonyl, 2-chlorobenzyloxycarbonyl, 2,4-dichlorobenzyl-oxycarbonyl, 4-bromobenzyloxycarbonyl, 3-bromobenzyloxycarbonyl, 4-nitrobenzyloxy-carbonyl, 4-cyanobenzyloxycarbonyl, 4-(decyloxy)benzyloxycarbonyl and the like; the benzoylmethylsulfonyl group, dithiasuccinoyl ("Dts"), the 2-(nitro)phenylsulfenyl group ("Nps"), the diphenyl-phosphine oxide group and like amino-protecting groups. The species of amino-protecting group employed is not critical so long as the derivatized amino group is stable to the conditions of the subsequent reaction(s) and can be removed at the appropriate point without disrupting the remainder of the compounds. Preferred amino-protecting groups are Boc, Cbz and Fmoc. Further examples of amino-protecting groups embraced by the above term are well known in organic synthesis and the peptide art and are described by, for example, T.W. Greene and P.G.M. Wuts, "Protective Groups in Organic Synthesis," 2nd ed., John Wiley and Sons, New York, NY, 1991, Chapter 7, M. Bodanzsky, "Principles of Peptide Synthesis," 1st and 2nd revised ed., Springer-Verlag, New York, NY, 1984 and 1993, and Stewart and Young, "Solid Phase Peptide Synthesis," 2nd ed., Pierce Chemical Co., Rockford, IL, 1984, each of which is incorporated herein by reference. The related term "protected amino" defines an amino group substituted with an amino-protecting group discussed above.

The term "protected guanidino" as used herein refers to an "amino-protecting group" on one or two of the guanidino nitrogen atoms. Examples of "protected guanidino" groups are described by T.W. Greene and P.G.M. Wuts; M. Bodanzsky; and Stewart and Young, supra.

The term "carboxy-protecting group" as used herein refers to one of the ester derivatives of the carboxylic acid group commonly employed to block or protect the carboxylic acid group while reactions are carried out on other functional groups on the compound. Examples of such carboxylic acid protecting groups include t-butyl, 4-nitrobenzyl, 4-methoxybenzyl, 3,4-dimethoxybenzyl, 2,4-dimethoxybenzyl, 2,4,6-trimethoxybenzyl, 2,4,6-trimethylbenzyl, pentamethylbenzyl, 3,4-methylenedioxybenzyl, benzhydryl, 4,4'-dimethoxytrityl, 4,4',4"-trimethoxytrityl, 2-phenylpropyl, trimethylsilyl, t-butyldimethylsilyl, phenacyl, 2,2,2-trichloroethyl, - (trimethylsilyl)ethyl, -(di(n-butyl)methylsilyl)ethyl, p- toluenesulfonylethyl, 4-nitrobenzylsulfonylethyl, allyl, cinnamyl, 1-(trimethylsilylmethyl)-propenyl and like moieties. The species of carboxy-protecting group employed is not critical so long as the derivatized carboxylic acid is stable to the conditions of subsequent reaction(s) and can be removed at the appropriate point without disrupting the remainder of the molecule. Further examples of these groups are found in E. Haslam, "Protective Groups in Organic Chemistry," J.G.W. McOmie, Ed., Plenum Press, New York, NY, 1973, Chapter 5, and T.W. Greene and P.G.M. Wuts, "Protective Groups in Organic Synthesis," 2nd ed., John Wiley and Sons, New York, NY, 1991, Chapter 5, each of which is incorporated herein by reference. A related term is "protected carboxy," which refers to a carboxy group substituted with one of the above carboxy-protecting groups.

The term "hydroxy-protecting group" refers to readily cleavable groups bonded to hydroxyl groups, such as the tetrahydropyranyl, 2-methoxypropyl, 1-ethoxyethyl, methoxymethyl, 2-methoxyethoxymethyl, methylthiomethyl, t-butyl, t-amyl, trityl, 4-methoxytrityl, 4,4'-dimethoxytrityl, 4,4',4"-trimethoxytrityl, benzyl, allyl, trimethylsilyl, (t-butyl)dimethylsilyl, 2,2,2-trichloroethoxycarbonyl groups and the like. The species of hydroxy-protecting groups is not critical so long as the derivatized hydroxyl group is stable to the conditions of subsequent reaction(s) and can be removed at the appropriate point without disrupting the remainder of the molecule. Further examples of hydroxy-protecting groups are described by C.B. Reese and E. Haslam, "Protective Groups in Organic Chemistry," J.G.W. McOmie, Ed., Plenum Press, New York, NY, 1973, Chapters 3 and 4, respectively, and T.W. Greene and P.G.M. Wuts, "Protective Groups in Organic Synthesis," 2nd ed., John Wiley and Sons, New York, NY, 1991, Chapters 2 and 3. Related terms are "protected hydroxy," and "protected hydoxymethyl" which refer to a hydroxy or hydroxymethyl substituted with one of the above hydroxy-protecting groups.

The term "C_1 to C_4 alkylthio" refers to sulfide groups such as methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, t-butylthio and like groups.

The term "C_1 to C_4 alkylsulfoxide" indicates sulfoxide groups such as methylsulfoxide, ethylsulfoxide, n-propylsulfoxide, isopropylsulfoxide, n-butylsulfoxide, sec-butylsulfoxide and the like.

The term "C_1 to C_4 alkylsulfonyl" encompasses groups such as methylsulfonyl, ethylsulfonyl, n-propylsulfonyl, isopropylsulfonyl, n-butylsulfonyl, t-butylsulfonyl and the like.

The terms "C_1 to C_4 substituted alkylthio," "C_1 to C_4 substituted alkylsulfoxide," and "C_1 to C_4 substituted alkylsulfonyl," denote the C_1 to C_4 alkyl portion of these groups may be substituted as described above in relation to "substituted alkyl."

The terms "phenylthio,"phenylsulfoxide," and "phenylsulfonyl" specify a thiol, a sulfoxide, or sulfone, respectively, containing a phenyl group. The terms "substituted phenylthio," "substituted phenylsulfoxide," and "substituted phenylsulfonyl" means that the phenyl of these groups can be substituted as described above in relation to "substituted phenyl."

The term "C_1 to C_6 alkylaminocarbonyl" means a C_1 to C_6 alkyl attached to a nitrogen of the aminocarbonyl group. Examples of C_1 to C_6 alkylaminocarbonyl include methylaminocarbonyl (from methylisocyanate), ethylaminocarbonyl (from ethylisocyanate), propylaminocarbonyl (from propylisocyanate), butylaminocarbonyl (from butylisocyatate). The term "C_1 to C_6 substituted alkylaminocarbonyl" denotes a substituted alkyl bonded to a nitrogen of the aminocarbonyl group, which alkyl may be substituted as described above in relation to C_1 to C_6 substituted alkyl. Examples of C_1 to C_6 substituted alkylaminocarbonyl include, for example, methoxymethylaminocarbonyl (from methoxymethylisocyanate), 2-chloroethylaminocarbonyl (from 2-chloroethylisocyanate), 2-oxopropylaminocarbonyl (from 2-oxopropylisocyanate), and 4-phenylbutylaminocarbonyl (from phenylbutylisocyanate).

The term "C_1 to C_7 alkoxycarbonyl" means a "C_1 to C_7 alkoxy" group attached to a carobonyl group. The term "C_1 to C_7 substituted alkoxycarbonyl" denotes a substituted alkoxy bonded to the carbonyl group, which

alkoxy may be substituted as described above in relation to C_1 to C_6 substituted alkyl.

The term "phenylaminocarbonyl" means a phenyl attached to a nitrogen of the aminocarbonyl group. The term "substituted phenylaminocarbonyl" denotes a substituted phenyl bonded to a nitrogen of the aminocarbonyl group, which phenyl may be substituted as described above in relation to substituted phenyl. Examples of substituted phenylaminocarbonyl include 2-chlorophenylaminocarbonyl (from 2-chlorophenylisocyanate), 3-chlorophenylaminocarbonyl (from 3-chlorophenylisocyanate), 2-nitorphenylaminocarbonyl (from 2-nitrophenylisocyanate), 4-biphenylaminocarbonyl (from 4-biphenylisocyanate), and 4-methoxyphenylaminocarbonyl (from 4-methoxyphenylisocyanate).

The term "C_1 to C_6 alkylaminothiocarbonyl" means a C_1 to C_6 alkyl attached to an aminothiocarbonyl group, wherein the alkyl has the same meaning as defined above. Examples of C_1 to C_6 alkylaminothiocarbonyl include methylaminothiocarbonyl (from methylisothiocyanate), ethylaminothiocarbonyl (from ethylisothiocyanate), propylaminothiocarbonyl (from propylisothiocyanate), butylaminothiocarbonyl (from butylisothiocyatate).

The term "C_1 to C_6 substituted alkylaminothiocarbonyl" denotes a substituted alkyl bonded to an aminothiocarbonyl group, wherein the alkyl may be substituted as described above in relation to C_1 to C_6 substituted alkyl. Examples of C_1 to C_6 substituted alkylaminothiocarbonyl include, for example, methoxymethylaminothiocarbonyl (from methoxymethylisothiocyanate), 2-chloroethylaminothiocarbonyl (from 2-chloroethylisothiocyanate),

2-oxopropylaminothiocarbonyl (from 2-oxopropylisothiocyanate), and 4-phenylbutylaminothiocarbonyl (from phenylbutylisothiocyanate).

The term "phenylaminothiocarbonyl" means a phenyl attached to an aminothiocarbonyl group, wherein the phenyl has the same meaning as defined above.

The term "substituted phenylaminothiocarbonyl" denotes a substituted phenyl bonded to an aminothiocarbonyl group, wherein phenyl may be substituted as described above in relation to substituted phenyl. Examples of substituted phenylaminothiocarbonyls include 2-chlorophenylaminothiocarbonyl (from 2-chlorophenylisothiocyanate), 3-chlorophenylaminothiocarbonyl (from 3-chlorophenylisothiocyanate), 2nitorphenylaminothiocarbonyl (from 2-nitrophenylisothiocyanate), 4-biphenylaminothiocarbonyl (from 4-biphenylisothiocyanate), and 4-methoxyphenylaminothiocarbonyl (from 4-methoxyphenylisothiocyanate).

The term "C_1 to C_{12} alkylene" means a C_1 to C_{12} alkyl group where the alkyl radical is bonded at two positions connecting together two separate additional groups. Examples of "C_1 to C_{12} alkylene" include methylene, 1,2-ethyl, 1,1-ethyl, 1,3-propyl.

The term "phenylene" means a phenyl group where the phenyl radical is bonded at two positions connecting together two separate additional groups. Examples of "phenylene" includes 1,2-phenylene, 1,3-phenylene, and 1,4-phenylene.

The term "substituted C_1 to C_{12} alkylene" means a C_1 to C_{12} alkyl group where the alkyl radical is bonded at two positions connecting together two separate additional groups and further bearing an additional substituent. Examples of "substituted C_1 to C_{12} alkylene" includes aminomethylene, 1-(amino)-1,2-ethyl, 2-(amino)-1,2-ethyl, 1-(acetamido)-1,2-ethyl, 2-(acetamido)-1,2-ethyl, 2-hydroxy-1,1-ethyl, 1-(amino)-1,3-propyl.

The term "substituted phenylene" means a phenyl group where the phenyl radical is bonded at two positions connecting together two separate additional groups, wherein the phenyl is substituted as described above in relation to "substituted phenyl." Examples of "substituted phenylene" include thoses derived from the building blocks, namely, 3-methyoxy-1,4-phenylene from 4-hydroxy-3-methoxybenzonitrile, 2-fluoro-1,4-phenylene from 2-fluoro-4-hydroxybenzonitrile, 3,5-Dibromo-1,4-phenylene from 3,5-dibromo-4-hydroxybenzonitrile, 3,5-diiodo-1,4-phenylene from 3,5-diiodo-4-hydroxybenzonitrile, 3,4-Dihydroxy-1,2-phenylene from 3,4-dihydroxybenzonitrile, 2,3,5,6-tetrafluoro-1,4-phenylene from 4-hydroxytetrafluorobenzonitrile, 3-bromo-4-hydroxy-1,2-phenylene from 3-bromo-4-hydroxy-benzonitrile, 3,5-di-tert-butyl-1,4-phenylene from 3,5-di-tert-butyl-4-hydroxybenzonitrile, 4-hydroxy-3-nitro-1,2-phenylene from 4-hydroxy-3-nitrobenzonitrile, 5-hydroxy-1,3-phenylene form 3,5-dihydroxybenzonitrile, 2-chloro-4-hydroxy-1,4-phenylene from 2-chloro-4-hydroxybenzonitrile, 2-fluoro-1,4-phenylene from 4-cyano-2-fluorophenol, 3,5-dimethyl-1,4-phenylene from 3,5-dimethyl-4-hydroxybenzonitrile, 2,6-dimethyl-1,4-phenylene from 2,6-dimethyl-4-hydroxybenzonitrile, 2,6 dichloro-1,4-phenylene from 2,6-dichloro-4-hydroxybenzonitrile, 4-chloro-1,2- phenylene from 4-chloro-2-hydroxybenzonitrile, 6-nitro-1,2-phenylene from 2-cyano-6-nitro-phenol, 5-nitro-1,2-phenylene from

2-hydroxy-5-nitrobenzonitrile, 2-amino-1,4-phenylene from 2-amino-4-cyanophenol, 2-carboxymethyl-1,4-phenylene from methyl-2-hydroxy-5-cyano-benzoate, 2-iodo-6-nitro-1,4-phenylene from 4-cyano-2-iodo-6-nitrophenol.

The terms "cyclic C_2 to C_7 alkylene," "substituted cyclic C_2 to C_7 alkylene," "cyclic C_2 to C_7 heteroalkylene," and "substituted cyclic C_2 to C_7 heteroalkylene," defines such a cyclic group bonded ("fused") to the phenyl radical resulting in a bicyclic ring system. The cyclic group may be saturated or contain one or two double bonds. Furthermore, the cyclic group may have one or two methylene or methine groups replaced by one or two oxygen, nitrogen or sulfur atoms which are the cyclic C_2 to C_7 heteroalkylene.

The cyclic alkylene or heteroalkylene group may be substituted once or twice by the same or different substituents selected from the group consisting of the following moieties: hydroxy, protected hydroxy, carboxy, protected carboxy, oxo, protected oxo, C_1 to C_4 acyloxy, formyl, C_1 to C_7 acyl, C_1 to C_6 alkyl, C_1 to C_7 alkoxy, C_1 to C_4 alkylthio, C_1 to C_4 alkylsulfoxide, C_1 to C_4 alkylsulfonyl, halo, amino, protected amino, (monosubstituted)amino, protected (monosubstituted)amino, (disubstituted)amino, hydroxymethyl or a protected hydroxymethyl.

The cyclic alkylene or heteroalkylene group fused onto the benzene radical can contain two to ten ring members, but it preferably contains three to six members. Examples of such saturated cyclic groups are when the resultant bicyclic ring system is 2,3-dihydro-indanyl and a tetralin ring. When the cyclic groups are unsaturated, examples occur when the resultant bicyclic ring system is a naphthyl ring or indolyl. Examples of fused cyclic groups which each contain one nitrogen atom

and one or more double bond, preferably one or two double bonds, are when the benzene radical is fused to a pyridino, pyrano, pyrrolo, pyridinyl, dihydropyrrolo, or dihydropyridinyl ring. Examples of fused cyclic groups which each contain one oxygen atom and one or two double bonds are when the benzene radical ring is fused to a furo, pyrano, dihydrofurano, or dihydropyrano ring. Examples of fused cyclic groups which each have one sulfur atom and contain one or two double bonds are when the benzene radical is fused to a thieno, thiopyrano, dihydrothieno or dihydrothiopyrano ring. Examples of cyclic groups which contain two heteroatoms selected from sulfur and nitrogen and one or two double bonds are when the benzene radical ring is fused to a thiazolo, isothiazolo, dihydrothiazolo or dihydroisothiazolo ring. Examples of cyclic groups which contain two heteroatoms selected from oxygen and nitrogen and one or two double bonds are when the benzene ring is fused to an oxazolo, isoxazolo, dihydrooxazolo or dihydroisoxazolo ring. Examples of cyclic groups which contain two nitrogen heteroatoms and one or two double bonds occur when the benzene ring is fused to a pyrazolo, imidazolo, dihydropyrazolo or dihydroimidazolo ring or pyrazinyl.

The term "carbamoyl" means an -NCO- group where the radical is bonded at two positions connecting two separate additional groups.

One or more of the compounds of the invention, even within a given library, may be present as a salt. The term "salt" encompasses those salts that form with the carboxylate anions and amine nitrogens and include salts formed with the organic and inorganic anions and cations discussed below. Furthermore, the term includes salts that form by standard acid-base reactions with basic groups (such as amino groups) and organic or inorganic acids. Such acids include hydrochloric,

sulfuric, phosphoric, acetic, succinic, citric, lactic, maleic, fumaric, palmitic, cholic, pamoic, mucic, D-glutamic, D-camphoric, glutaric, phthalic, tartaric, lauric, stearic, salicyclic, methanesulfonic, benzenesulfonic, sorbic, picric, benzoic, cinnamic, and like acids.

The term "organic or inorganic cation" refers to counter-ions for the carboxylate anion of a carboxylate salt. The counter-ions are chosen from the alkali and alkaline earth metals, (such as lithium, sodium, potassium, barium, aluminum and calcium); ammonium and mono-, di- and tri-alkyl amines such as trimethylamine, cyclohexylamine; and the organic cations, such as dibenzylammonium, benzylammonium, 2-hydroxyethylammonium, bis(2-hydroxyethyl)ammonium, phenylethylbenzylammonium, dibenzylethylenediammonium, and like cations. See, for example, "Pharmaceutical Salts," Berge et al., J. Pharm. Sci., 66:1-19 (1977), which is incorporated herein by reference. Other cations encompassed by the above term include the protonated form of procaine, quinine and N-methylglucosamine, and the protonated forms of basic amino acids such as glycine, ornithine, histidine, phenylglycine, lysine and arginine. Furthermore, any zwitterionic form of the instant compounds formed by a carboxylic acid and an amino group is referred to by this term. For example, a cation for a carboxylate anion will exist when R_2 or R_3 is substituted with a (quaternary ammonium)methyl group. A preferred cation for the carboxylate anion is the sodium cation.

The compounds of the invention can also exist as solvates and hydrates. Thus, these compounds may crystallize with, for example, waters of hydration, or one, a number of, or any fraction thereof of molecules of the mother liquor solvent. The solvates and hydrates of

such compounds are included within the scope of this invention.

One or more compounds of the invention, even when in a library, can be in the biologically active ester form, such as the non-toxic, metabolically-labile ester-form. Such ester forms induce increased blood levels and prolong the efficacy of the corresponding non-esterified forms of the compounds. Ester groups which can be used include the lower alkoxymethyl groups, for example, methoxymethyl, ethoxymethyl, isopropoxymethyl and the like; the -(C_1 to C_7) alkoxyethyl groups, for example methoxyethyl, ethoxyethyl, propoxyethyl, isopropoxyethyl and the like; the 2-oxo-1,3-diooxlen-4-ylmethyl groups, such as 5-methyl-2-oxo-1,3-dioxolen-4-ylmethyl, 5-phenyl-2-oxo-1,3-dioxolen-4-ylmethyl and the like; the C_1 to C_4 alkylthiomethyl groups, for example methylthiomethyl, ethylthiomethyl, iso-propylthiomethyl and the like; the acyloxymethyl groups, for example pivaloyloxymethyl, pivaloyloxyethyl, -acetoxymethyl and the like; the ethoxycarbonyl-1-methyl group; the -acetoxyethyl; the 1-(C_1 to C_7 alkyloxycarbonyloxy)ethyl groups such as the 1-(ethoxycarbonyloxy)ethyl group; and the 1-(C_1 to C_7 alkylaminocarbonyloxy)ethyl groups such as the 1-(methylaminocarbonyloxy)ethyl group.

The term "amino acid" includes any one of the twenty naturally-occurring amino acids or the D-form of any one of the naturally-occurring amino acids. In addition, the term "amino acid" also includes other non-naturally occurring amino acids besides the D-amino acids, which are functional equivalents of the naturally-occurring amino acids. Such non-naturally-occurring amino acids include, for example, norleucine ("Nle"), norvaline ("Nva"), L- or D- naphthalanine, ornithine ("Orn"), homoarginine (homoArg) and others well known in the peptide art, such as those described in M. Bodanzsky,

"Principles of Peptide Synthesis," 1st and 2nd revised ed., Springer-Verlag, New York, NY, 1984 and 1993, and Stewart and Young, "Solid Phase Peptide Synthesis," 2nd ed., Pierce Chemical Co., Rockford, IL, 1984, both of which are incorporated herein by reference. Amino acids and amino acid analogs can be purchased commercially (Sigma Chemical Co.; Advanced Chemtech) or synthesized using methods known in the art.

The term "functionalized resin" means any resin, crosslinked or otherwise, where functional groups have been introduced into the resin, as is common in the art. Such resins include, for example, those functionalized with amino, alkylhalo, formyl or hydroxy groups. Such resins which can serve as solid supports are well known in the art and include, for example, 4-methylbenzhydrylamine-copoly(styrene-1% divinylbenzene) (MBHA), 4-hydroxymethylphenoxymethyl-copoly(styrene-1% divinylbenzene), 4-oxymethyl-phenyl-acetamido-copoly(stryene-1% divinylbenzene)(Wang), 4-(oxymethyl)-phenylacetamido methyl (Pam), and Tentagel™, from Rapp Polymere Gmbh, trialkoxy-diphenyl-methyl ester-copoly(styrene-1% divinylbenzene)(RINK) all of which are commercially available. Other functionalized resins are known in the art and can be use without departure from the scope of the current invention. Such resins may include those described in Jung, G., Combinatorial Peptide and Nonpeptide Libraties, A Handbook (VCH Verlag, 1996) or Bunin, B. A., The Combinatorial Index (Academic Press, 1998) and are incorporated herein by reference.

As used herein, a "combinatorial library" is an intentionally created collection of differing molecules which can be prepared by the means provided below or otherwise and screened for biological activity in a variety of formats (e.g., libraries of soluble molecules, libraries of compounds attached to resin beads, silica

chips or other solid supports). A "combinatorial library," as defined above, involves successive rounds of chemical syntheses based on a common starting structure. The combinatorial libraries can be screened in any variety of assays, such as those detailed below as well as others useful for assessing their biological activity. The combinatorial libraries will generally have at least one active compound and are generally prepared such that the compounds are in equimolar quantities.

Compounds disclosed in previous work that are not in a mixture are not part of a "combinatorial library" of the invention. In addition, compounds that are in an unintentional or undesired mixture are not part of a "combinatorial library" of the invention.

A combinatorial library of the invention can contain two or more of the above-described compounds. The invention further provides a combinatorial library containing five or more of the above-described compounds. In another embodiment of the invention, a combinatorial library can contain ten or more of the above-described compounds. In yet another embodiment of the invention, a combinatorial library can contain fifty or more of the above-described compounds. If desired, a combinatorial library of the invention can contain 100,000 or more, or even 1,000,000 or more, of the above-described compounds.

By way of example, the preparation of the combinatorial libraries can use the "split resin approach." The split resin approach is described by, for example, U.S. Patent 5,010,175 to Rutter, WO PCT 91/19735 to Simon, and Gallop et al., *J. Med. Chem.*, 37:1233-1251 (1994), all of which are incorporated herein by reference.

The amino acids are indicated herein by either their full name or by the commonly known three letter code. Further, in the naming of amino acids, "D-" designates an amino acid having the "D" configuration, as opposed to the naturally occurring L-amino acids. Where no specific configuration is indicated, one skilled in the art would understand the amino acid to be an L-amino acid. The amino acids can, however, also be in racemic mixtures of the D- and L-configuration or the D-amino acid can readily be substituted for that in the L-configuration.

For preparing pharmaceutical compositions containing compounds of the invention, inert, pharmaceutically acceptable carriers are used. The pharmaceutical carrier can be either solid or liquid. Solid form preparations include, for example, powders, tablets, dispersible granules, capsules, cachets, and suppositories.

A solid carrier can be one or more substances which can also act as diluents, flavoring agents, solubilizers, lubricants, suspending agents, binders, or tablet disintegrating agents; it can also be an encapsulating material.

In powders, the carrier is generally a finely divided solid which is in a mixture with the finely divided active component. In tablets, the active compound is mixed with the carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired.

For preparing pharmaceutical composition in the form of suppositories, a low-melting wax such as a mixture of fatty acid glycerides and cocoa butter is first melted and the active ingredient is dispersed

therein by, for example, stirring. The molten homogeneous mixture is then poured into convenient-sized molds and allowed to cool and solidify.

Powders and tablets preferably contain between about 5% to about 70% by weight of the active ingredient. Suitable carriers include, for example, magnesium carbonate, magnesium stearate, talc, lactose, sugar, pectin, dextrin, starch, tragacanth, methyl cellulose, sodium carboxymethyl cellulose, a low-melting wax, cocoa butter and the like.

The pharmaceutical compositions can include the formulation of the active compound with encapsulating material as a carrier providing a capsule in which the active component (with or without other carriers) is surrounded by a carrier, which is thus in association with it. In a similar manner, cachets are also included. Tablets, powders, cachets, and capsules can be used as solid dosage forms suitable for oral administration.

Liquid pharmaceutical compositions include, for example, solutions suitable for oral or parenteral administration, or suspensions, and emulsions suitable for oral administration. Sterile water solutions of the active component or sterile solutions of the active component in solvents comprising water, ethanol, or propylene glycol are examples of liquid compositions suitable for parenteral administration.

Sterile solutions can be prepared by dissolving the active component in the desired solvent system, and then passing the resulting solution through a membrane filter to sterilize it or, alternatively, by dissolving the sterile compound in a previously sterilized solvent under sterile conditions.

Aqueous solutions for oral administration can be prepared by dissolving the active compound in water and adding suitable flavorants, coloring agents, stabilizers, and thickening agents as desired. Aqueous suspensions for oral use can be made by dispersing the finely divided active component in water together with a viscous material such as natural or synthetic gums, resins, methyl cellulose, sodium carboxymethyl cellulose, and other suspending agents known to the pharmaceutical formulation art.

Preferably, the pharmaceutical composition is in unit dosage form. In such form, the composition is divided into unit doses containing appropriate quantities of the active Oxadiazole. The unit dosage form can be a packaged preparation, the package containing discrete quantities of the preparation, for example, packeted tablets, capsules, and powders in vials or ampules. The unit dosage form can also be a capsule, cachet, or tablet itself, or it can be the appropriate number of any of these packaged forms.

As pharmaceutical compositions for treating infections, pain, or any other indication the compounds of the present invention are generally in a pharmaceutical composition so as to be administered to a subject at dosage levels of from 0.7 to 7000 mg per day, and preferably 1 to 500 mg per day, for a normal human adult of approximately 70 kg of body weight, this translates into a dosage of from 0.01 to 100 mg/kg of body weight per day. The specific dosages employed, however, can be varied depending upon the requirements of the patient, the severity of the condition being treated, and the activity of the compound being employed. The determination of optimum dosages for a particular situation is within the skill of the art.

The compounds of Formula (I) and combinatorial libraries containing the same can be prepared as set forth in the Reaction Schemes provided in the Reaction Schemes 2 through 5 and described below.

Several variant oxadiazole combinatorial libraries have been prepared in order to achieve a high level of diversity. Different types of nitrile containing substrates were attached to solid support. Among the available nitriles, those containing a carboxylic acid moiety were coupled to a resin-bound amine via an amide bond (Scheme 1: Attachment of Cyanocarboxylic acids to solid support). The carboxylic acid was coupled directly to a resin bound primary amine such as methyl benzhydrylamine (MBHA), or RINK amide linker or other resins known in the art which afford a primary amide functional group after cleavage. Alternatively the cyano carboxylic acids were coupled to resin-bound primary or secondary amines which become incorporated into the product as secondary or tertiary amides after cleavage from the resin. These could be prepared by reductive amination of a primary amine to an aldehyde resin or vice-versa, or to any other resin-bound primary or secondary amine prepared by methods known to those skilled in the art.

Cyanophenols were coupled to solid support via an ether linkage as shown in Scheme 2: Attachment of cyanophenols to solid support which releases the free phenol after cleavage, by alkylation of a benzyl halide resin such as Merrifield resin or alkoxybenzyl bromide resin (Wang bromide resin). Alternatively, the cyanophenols were coupled to an alkyl halide moiety which remains covalently attached to the oxadiazole product after cleavage from the resin. For example, a primary or secondary amine bound to the resin through a cleavable linker is acylated with chloroacetic anhydride or 3- or

4-chloromethyl benzoic acid. A cyanophenol was then introduced by nucleophilic displacement of the alkyl halide. In this way, a wide range of cyanophenyl compounds was made, and converted to oxadiazole compounds by the methods described below.

Other types of nitrile containing compounds can be similarly linked to common resins as shown in Scheme 3: Linking nitriles to solid support. For example, 3-cyanophenyl isocyanate and 4-cyanophenyl isocyanate were linked to the resin by forming a urea linkage and the nitrile function elaborated into an oxadiazole. Additionally, cyanohydrins may be formed on the resin by the action of Trimethylsilyl cyanide on resin-bound aldehydes and ketones. Alkyl nitriles may be formed by displacement of leaving groups with cyanide anion. Primary and secondary amines attached to the resin were alkylated with 3- and 4-cyanobenzylbromide, and the cyanobenzylamines converted to oxadiaxoles. Because of the relatively low number of suitable commercially available nitriles, N-Boc 2-cyanoethyl glycine was also found to be a useful precursor to a large number of oxadiazole derivatives. The cyanoethyl group was first converted to the oxadiazole followed by conversion of the Boc-protected amine to a variety of derivatives.

In order to provide further diversity, conversion of the nitrile function into the oxadiazole ring was done following a number of methods (Scheme 4: Conversion of Nitriles into Oxadiazoles). Treatment of the nitriles with hydroxylamine in alcohol solvent provided the amidoximes in quantitative yield. The amidoximes were then treated with different types of acylating agents to give 3,5-substituted oxadiazoles. In a first embodiment, the amidoximes were treated with trichloroacetic anhydride to give the 5-trichloromethyl derivatives which were further reacted with secondary

amines to give 5-amino oxadiazoles by displacement of the trichloromethyl group. Alternatively, the amidoximes were treated with chloroacetic anhydride to give the 5-chloromethyl oxadiazoles. This primary chloride could be displaced with diverse primary or secondary amines to give substituted 2% or 3% amines. These could be derivatized further to introduce an additional variable substituent. This strategy was particularly useful for the preparation of compounds attached to the resin by TFA labile bonds which preclude the use of N-Boc-protected amino acids (vide infra). This was also the method of choice with cyanoethyl glycine derivatives. Third, the amidoximes were converted to oxadiazoles by reaction with BOC amino acid anhydrides or FMOC amino acid anhydrides to give the substituted oxadiazole derivatives. Natural L-amino acid derivatives (e.g. Gly, Phe, Leu) were used as well as D- or L-amino acids, cyclic amino acids (e.g. Pro, Nipecotic acid, Isonipecotic acid, tetrahydroisoquinoline carboxylic acid), unnatural amino acids, or other aliphatic carboxylic acids and anhydrides. In all cases, the carboxylic acid moiety becomes incorporated into the oxadiazole ring.

Furthermore, the N-BOC or N-FMOC protecting group could be removed under standard conditions and the resulting amine derivatized with an additional diverse set of reagents (Scheme 5: Derivatization of Oxadiazoles). For example amide, sulfonamide, urea and thiourea derivatives were obtained by reaction with acid anhydride, sulfonyl chloride, isocyanates and isothiocyanates respectively. Fourth, the amidoximes can be reacted with activated carboxylic acid derivatives other than anhydrides. Any acylating reagent known in the art could be used in the synthesis of oxadiazoles, including but not limited to acid chlorides, and fluorides, mixed anhydrides, active esters such as

pentafluorophenyl, 4-nitrophenyl, hydroxybenzotriazole, N-hydroxysuccinimide and the like.

In general, large diverse combinatorial libraries of oxadiazole compounds were prepared by assembling the three sets of building blocks in all possible permutations. Thus the libraries are described as having three variable positions, or three diversity sites. In one embodiment of these methods, the first diversity site is defined by the nitrile containing moiety, or its precursor, attached to the resin. This includes, but is not limited to, cyanocarboxylic acids, cyanobenzyl halides and cyanophenols, and the coupling of these through appropriate chemistry to diverse compounds on solid support. Additionally, these methods are meant to include as starting materials other products synthesized on solid phase whereby an aliphatic, aromatic or heteroaromatic nitrile compound is obtained. The second diversity site is introduced in the oxadiazole formation and is defined by the appropriately functionalized carboxylic acid anhydride used in the cyclization step. The third diversity site is created by the derivatization of a reactive site introduced by the carboxylic acid moiety in the previous step. More specifically, the use of protected amino acid derivatives is particularly useful in the present invention. The amino acid side chain provides the second diversity site as defined above. Derivatization of the amino group with carboxylic acids, sulfonyl chlorides, isocyanates, isothiocyanates, alkyl halides or aldehydes provides the third diversity site. Other reactive functional groups incorporated in protected or unprotected form can also serve to introduce the third diversity element. In another embodiment of the invention, bifunctional carboxylic acid derivatives are used to form the oxadiazole ring and an attachment point for a third diversity site. This attachment point can be a

nucleophilic site (e.g. alcohol, thiol, carbon nucleophile, etc.) or an electrophilic site (halide, tosylate, triflate, activated carboxylate, etc). In particular, cyclic anhydrides such as succinic anhydride, diglycolic anhydride, 1,2-cyclopropane dicarboxylic anhydride are preferred embodiments. The oxadiazole cyclization produces a pendant carboxylic acid which can be further activated with standard coupling reagents and coupled to diverse amines. Another preferred embodiment of the invention is the use of chloroacetic anhydride or other halocarboxylic acid anhydrides in the oxadiazole cyclization creating a chloromethyl group which is readily displaced with diverse nucleophiles such as amines, thiols, alcohols, phenols or carbon nucleophiles. In a most preferred embodiment primary amines or secondary diamines are used which are derivatized further with carboxylic acids, sulfonyl chlorides, isocyanates, isothiocyanates or alkyl halides.

The synthesis of oxadiazoles on solid support could also be performed in the opposite orientation. A carboxylic acid moiety could be attached to the solid support in a variety of different ways, for example, an amino acid ester is attached to a resin by reductive amination, or by reaction with a chloroformate resin derivative, followed by hydrolysis of the ester. Alternatively, a resin bound amine can be reacted with a cyclic anhydride such as succinic anhydride. Other methods of providing a free carboxylic acid on solid support are known in the art. The carboxylic acid is then converted to an activated derivative such as the mixed anhydride with isobutyl chloroformate, or an active ester with pentafluorophenol, 4-nitrophenol, N-hydroxysuccinimide, HOBT or other activated derivatives such as those used routinely in the formation of amide or ester bonds. This activated resin bound carboxylate is then treated immediately with a solution of amidoxime,

prepared by the reaction of a nitrile compound with hydroxylamine under standard conditions.

The nonsupport-bound combinatorial libraries can be screened as mixtures in solution in assays such as radio-receptor inhibition assays, anti-bacterial assays, anti-fungal assays, calmodulin-dependent phosphodiesterase (CaMPDE) assays and phosphodiesterase (PDE) assays, as described in detail below. Deconvolution of highly active mixtures can then be carried out by iterative or positional scanning methods. These techniques, the iterative approach or the positional scanning approach, can be utilized for finding other active compounds within the combinatorial libraries of the present invention using any one of the below-described assays or others well known in the art.

The iterative approach is well-known and is set forth in general in Houghten *et al.*, *Nature*, 354, 84-86 (1991) and Dooley *et al.*, *Science*, 266, 2019-2022 (1994), both of which are incorporated herein by reference. In the iterative approach, for example, sub-libraries of a molecule having three variable groups are made wherein the first variable is defined. Each of the compounds with the defined variable group is reacted with all of the other possibilities at the other two variable groups. These sub-libraries are each tested to define the identity of the second variable in the sub-library having the highest activity in the screen of choice. A new sub-library with the first two variable positions defined is reacted again with all the other possibilities at the remaining undefined variable position. As before, the identity of the third variable position in the sub-library having the highest activity is determined. If more variables exist, this process is repeated for all variables, yielding the compound with each variable contributing to the highest desired activity in the

screening process. Promising compounds from this process can then be synthesized on larger scale in traditional single-compound synthetic methods for further biological investigation.

The positional-scanning approach has been described for various combinatorial libraries as described, for example, in R. Houghten *et al.* PCT/US91/08694 and U.S. Patent 5,556,762, both of which are incorporated herein by reference. In the positional scanning approach, sublibraries are made defining only one variable with each set of sublibraries and all possible sublibraries with each single variable defined (and all other possibilities at all of the other variable positions), made and tested. From the instant description one skilled in the art could synthesize combinatorial libraries wherein two fixed positions are defined at a time. From the testing of each single-variable defined combinatorial library, the optimum substituent at that position can be determined, pointing to the optimum or at least a series of compounds having a maximum of the desired biological activity. Thus, the number of sublibraries for compounds with a single position defined will be the number of different substituents desired at that position, and the number of all the compounds in each sublibrary will be the product of the number of substituents at each of the other variables.

Individual compounds and pharmaceutical compositions containing the compounds, as well as methods of using the same, are included within the scope of the present invention. The compounds of the present invention can be used for a variety of purposes and indications and as medicaments for any such purposes and indications. For example, as described above, compounds of the present invention, including oxadiazole

derivatives, can be used as pesticides, acaricides, receptor agonisits and antiviral agents. Additionally, the subject compounds can be useful as analgesics. Assays which can be used to test the biological activity of the instant compounds include antimicrobial assays, a competitive enzyme-linked immunoabsorbent assay and radio-receptor assays, as described below.

The ability of the compounds to inhibit bacterial growth, and therefore be useful to that infection, can be determined by methods well known in the art. Compounds of the present invention were shown to have antimicrobial activity by the *in vitro* antimicrobial activity assay described in Example 36 below and, therefore, are useful as antimicrobial agents.

In addition, an exemplary *in vitro* antimicrobial activity assay is described in Blondelle and Houghten, *Biochemistry* 30:4671-4678 (1991), which is incorporated herein by reference. In brief, *Staphylococcus aureus* ATCC 29213 (Rockville, MD) is grown overnight at 37°C in Mueller-Hinton broth, then re-inoculated and incubated at 37°C to reach the exponential phase of bacterial growth (i.e., a final bacterial suspension containing 10^5 to 5 x 10^5 colony-forming units/ml). The concentration of cells is established by plating 100 µl of the culture solution using serial dilutions (e.g., 10^{-2}, 10^{-3} and 10^{-4}) onto solid agar plates. In 96-well tissue culture plates, compounds, individual or in mixtures, are added to the bacterial suspension at concentrations derived from serial two-fold dilutions ranging from 1500 to 2.9 µg/ml. The plates are incubated overnight at 37°C and the growth determined at each concentration by OD_{620} nm. The IC_{50} (the concentration necessary to inhibit 50% of the growth of the bacteria) can then be calculated.

The competitive ELISA method which can be used here is a modification of the direct ELISA technique described previously in =Appel et al., J. Immunol. 144:976-983 (1990), which is incorporated herein by reference. It differs only in the MAb addition step. Briefly, multi-well microplates are coated with the antigenic peptide (Ac-GASPYPNLSNQQT-NH_2) at a concentration of 100 pmol/50 μl. After blocking, 25 μl of a 1.0 mg/ml solution of each mixture of a synthetic combinatorial library (or individual compound) is added, followed by MAb 125-10F3 (Appel et al., *supra*) (25 μl per well). The MAb is added at a fixed dilution in which the bicyclic guanidine in solution effectively competes for MAb binding with the antigenic peptide adsorbed to the plate. The remaining steps are the same as for direct ELISA. The concentration of compound necessary to inhibit 50% of the MAb binding to the control peptide on the plate (IC_{50}) is determined by serial dilutions of the compound.

Alternative screening can be done with radio-receptor assays. The radio-receptor assay, can be selective for any one of the μ, κ, or δ opiate receptors. Compounds of the present invention can be useful in vitro for the diagnosis of relevant opioid receptor subtypes, such as κ, in the brain and other tissue samples. Similarly, the compounds can be used *in vivo* diagnostically to localize opioid receptor subtypes.

The radio-receptor assays are also an indication of the compounds' analgesic properties as described, for example, in Dooley et al., *Proc. Natl. Acad. Sci.*, 90:10811-10815 (1993). For example, it can be envisioned that these compounds can be used for therapeutic purposes to block the peripheral effects of a centrally acting pain killer. For instance, morphine is

a centrally acting pain killer. Morphine, however, has a number of deleterious effects in the periphery which are not required for the desired analgesic effects, such as constipation and pruritus (itching). While it is known that the many compounds do not readily cross the blood-brain barrier and, therefore, elicit no central effect, the subject compounds can have value in blocking the periphery effects of morphine, such as constipation and pruritus. Accordingly, the subject compounds can also be useful as drugs, namely as analgesics, or to treat pathologies associated with other compounds which interact with the opioid receptor system.

Additionally, such compounds can be tested in a σ receptor assay. Ligands for the σ receptor can be useful as antipsychotic agents, as described in Abou-Gharbia et al., *Annual Reports in Medicinal Chemistry*, 28:1-10 (1993).

Radio-receptor assays can be performed with particulate membranes prepared using a modification of the method described in Pasternak et al., *Mol. Pharmacol.* 11:340-351 (1975), which is incorporated herein by reference. Rat brains frozen in liquid nitrogen can be obtained from Rockland (Gilbertsville, PA). The brains are thawed, the cerebella removed and the remaining tissue weighed. Each brain is individually homogenized in 40 ml Tris-HCl buffer (50 mM, pH 7.4, 4°C) and centrifuged (Sorvall® RC5C SA-600: Du Pont, Wilmington, DE) (16,000 rpm) for 10 minutes. The pellets are resuspended in fresh Tris-HCl buffer and incubated at 37°C for 40 minutes. Following incubation, the suspensions are centrifuged as before, the resulting pellets resuspended in 100 volumes of Tris buffer and the suspensions combined. Membrane suspensions are prepared and used in the same day. Protein content of the crude homogenates generally range from 0.15-0.2 mg/ml as

determined using the method described in Bradford, M.M., *Anal. Biochem.* 72:248-254 (1976), which is incorporated herein by reference.

Binding assays are carried out in polypropylene tubes, each tube containing 0.5 ml of membrane suspension. 8 nM of ^{3}H-[D-Ala^2,Me-Phe^4,Gly-ol^5]enkephalin (DAMGO) (specific activity = 36 Ci/mmol, 160,000 cpm per tube; which can be obtained from Multiple Peptide Systems, San Diego, CA, through NIDA drug distribution program 271-90-7302) and 80 μg/ml of bicyclic guanidine, individual or as a mixture and Tris-HCl buffer in a total volume of 0.65 ml. Assay tubes are incubated for 60 mins. at 25°C. The reaction is terminated by filtration through GF-B filters on a Tomtec harvester (Orange, CT). The filters are subsequently washed with 6 ml of Tris-HCl buffer, 4°C. Bound radioactivity is counted on a Pharmacia Biotech Betaplate Liquid Scintillation Counter (Piscataway, NJ) and expressed in cpm. To determine inter- and intra-assay variation, standard curves in which ^{3}H-DAMGO is incubated in the presence of a range of concentrations of unlabeled DAMGO (0.13-3900 nM) are generally included in each plate of each assay (a 96-well format). Competitive inhibition assays are performed as above using serial dilutions of the bicyclic guanidines, individually or in mixtures. IC_{50} values (the concentration necessary to inhibit 50% of ^{3}H-DAMGO binding) are then calculated. IC_{50} values of less than 1000 nM are indicative of highly active opioid compounds which bind to the μ receptor, with particularly active compounds having IC_{50} values of 100 nM or less and the most active compounds with values of less than 10 nM.

As opposed to this μ receptor selective assay, which can be carried out using ^{3}H-DAMGO as radioligand, as described above, assays selective for κ receptors can be carried out using [^{3}H]-U69,593 (3 nM, specific activity 62

Ci/mmol) as radioligand. Assays selective for δ opiate receptors can be carried out using tritiated DSLET ([D-Ser^2, D-Leu^5]-threonine-enkephalin) as radioligand. Assays selective for the σ opiate receptor can use radiolabeled pentazocine as ligand.

Screening of combinatorial libraries and compounds of the invention can be done with an anti-fungal assay. Compounds of the present invention can be useful for treating fungal infections.

Screening of combinatorial libraries and compounds of the invention also can be done with a calmodulin-dependent phosphodiesterase (CaMPDE) assay. Compounds of the present invention can be useful as calmodulin antagonists.

Calmodulin (CaM), which is the major intracellular calcium receptor, is involved in many processes that are crucial to cellular viability. In particular, calmodulin is implicated in calcium-stimulated cell proliferation. Calmodulin antagonists are, therefore, useful for treating conditions associated with increased cell proliferation, for example, cancer. In addition, calmodulin antagonists such as compounds of the subject invention are useful both in vitro and in vivo for identifying the role of calmodulin in other biological processes. The disadvantages of known antagonists such as trifluoperazine and N-(4-aminobutyl)-5-chloro-2-naphthalenesulfonamide (W13) include their non-specificity and toxicity. In contrast, advantages of the combinatorial libraries and compounds of the subject invention as calmodulin antagonists include their reduced flexibility and ability to generate broader conformational space of interactive residues as compared to their linear counterparts.

An example of an assay that identifies CaM antagonists is a CaMPDE assay. In brief, samples are mixed with 50 μl of assay buffer (360 mM Tris, 360 mM Imidazole, 45 mM $Mg(CH_3COO)_2$, pH 7.5) and 10 μl of $CaCl_2$ (4.5 mM) to a final volume of 251 μl. 25 μl of calmodulin stock solution (Boehringer Mannheim; 0.01 μg/μl) is then added and the samples then sit at room temperature for 10 minutes. 14 μl of PDE (Sigma; 2 Units dissolved in 4 ml of water; stock concentration: 0.0005 Units/μl) is then added, followed by 50 μl of 5'-nucleotidase (Sigma; 100 Units dissolved in 10 ml of 10 mM Tris-HCl containing 0.5 mM $Mg(CH_3COO)_2$, pH 7.0; stock concentration: 10 Units/ml). The samples are then incubated for 10 minutes at 30°C. 50 μl of adenosine 3',5'-cyclic monophosphate (cAMP) (20 mM in water at pH 7.0) is added, the samples incubated for 1 hour at 30°C and then vortexed. 200 μl of trichloroacetic acid (TCA) (55% in water) is added to a 200 μl sample aliquot, which is then vortexed and centrifuged for 10 minutes. 80 μl of the resulting supernatants of each sample is transferred to a 96-well plate, with 2 wells each containing 80 μl of each sample. 80 μl of ammonium molybdate (1.1% in 1.1N H_2SO_4) is then added to all the wells, and the OD of each were determined at 730nm, with the values later subtracted to the final OD reading. 16 μl of reducing agent (6g sodium bisulfite, 0.6g sodium sulfite and 125mg of 1-amino-2-naphtol-4-sulfonic acid in 50ml of water) is then added to one of each sample duplicate and 16 μl of water is added to the other duplicate. After sitting for 1 hour at room temperature, the OD of each well is determined at 730nm. The percent inhibition of calmodulin activity is then calculated for each sample, using as 0% inhibition a control sample containing all reagents without any test samples and as 100% inhibition a control sample containing test samples and all reagents except calmodulin. In addition, the percent inhibition of phosphodiesterase activity was

determined by following a similar protocol as the CaMPDE assay described above, except not adding calmodulin to the sample mixture and calculating the percent inhibition by using as 0% inhibition a control reagent without any test samples and as 100% inhibition a control sample containing test samples and all reagents except cAMP.

EXAMPLES

Experimental Procedures

The following Examples are intended to illustrate but not limit the present invention. The following abbreviations are used the following experimental procedures and examples: DMA, dimethyl acetamide; RT, room temperature; DMF, dimethylforamide; IPA, isopropyl alcohol; Wang resin, *p*-benzyloxybenzylalcohol-polystyrene; DCM, dichloromethane; MTBE, methyl-tert-butyl ether; MBHA-HCl resin, methyl-benzhydrylamine hydrochloride; PP, polypropylene; DIEA, diisopropylethylamine; HOBT, 1-hydroxybenzotriazole; DIC, N,N'-diisopropylcarbodiimide; DMAP, 4-dimethylamino-pyridine; KotBu, potassium tert-butoxide; Boc, tert-butoxycarbonyl; FMOC, 9-fluorenyl-methoxycarbonyl; Tos, *p*- toluenesulfonyl; Bzl, benzyl; For, formyl; PMC, 2,2,5,7,8-pentamethylchroman-6-sulfonyl; TBU, 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate; TRT, trityl; ACM, acetamidomethyl; MTR, 2,3,6-trimethyl-4-methoxybenzenesulfonyl; MBH, 4,4'-dimethoxybenzyhydryl; ADA, adamanyl; PMEOBZL, p-methoxybenzyl; 2-CL-Z, 2-chlorobenzyl-oxycarbonyl; 2-BR-Z, 2-bromobenzyloxycarbonyl; TMOB, 2,4,6-trimethoxybenzyl; MTT, 4-methyltrityl; PBF, 2,2,4,6,7- pentamethyldihydrobenzofuran-5-sulfonyl; DDE, 1-(4,4- dimethyl-2,6-dioxocyclohex-1-ylidene)ethyl; DMAB, 4-[N-(1- [4,4-diemthyl-2,6-dioxocyclhexylidene]-3-methylbutyl)-amino]benzzyl; TFA, trifluoroacetic acid;

BOP, benzotriazol- 1-yl-oxy-tris(dimethylamino)-phosphonium hexafluoro-phosphate; PyBOP, benzotriazol-1-yl-oxy-tris-pyrrolidino-phosphonium hexafluorophosphate; HATU, azabenzotriazolyl-N,N,N',N'-tetramethyluronium hexafluorophosphate; HBTU, 2- (1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate; MeOH, methanol; ACN, acetonitrile; DCE, 1,2-dichloroethane; THF, tetrahydrofuran; HF, hydrogen fluoride; HPLC/MS, high performance liquid chromatography - mass spectrometry; FIA-MS, flow injection analysis - mass spectrometry; ELSD, evaporative light scattering detector; THB, Todd Hewitt Broth; OD, optical density; DMSO, dimethylsulfoxide.

EXAMPLE 1

Synthesis of 4-alkoxy-2-methoxybenzaldehyde resin (DAB resin)

Chloromethyl polystyrene (500 g, 1.48 mmol/g, 740 mmol) was swollen in Dimethyl acetamide. 4-hydroxy-2-methoxybenzaldehyde (250g, 1645 mmol) was dissolved in 400 ml DMA and potassium t-butoxide was added (185 g, 1645 mmol) in portions. The green solution was added to the loose resin and the suspension was shaken overnight at 50 %C. The solution was cooled to RT, and the resin transfered to teabags washed with 2 l portions of DMF (1X), and 5%, 10% and 20% H2O in DMF (4X each), IPA and MeOH (3X). The resin was dried, to give 4-alkoxy-2-methoxybenzaldehyde polystyrene resin.

EXAMPLE 2

Preparation of Wang bromide resin

Wang resin (20 g, 24 mmol) was swollen in DCM. A solution of triphenylphosphine dibromide (30.4g, 72 mmol) in 500 ml DCM was added and the solution shaken for 3 hours or overnight. The resin was washed with DCM and

MTBE and dried under vacuum, to give 4-alkoxybenzyl bromide polystyrene resin.

EXAMPLE 3

Coupling of Nitrile Carboxylic acids to MBHA Resin

MBHA-HCl resin (Methylbenzhydrylamine Hydrochloride) (125 g, 162.5 mmol NH2) was dispensed into 15 10X15 cm PP mesh bags (8.33 g/bag). The resin was washed 3X with 5% DIEA/ DCM then 2X with DCM. The carboxylic acids below were dissolved in 500 ml DCM in separate Nalgene bottles, DIEA (28.3 ml, 162.5 mmol) and HOBT (24.9 g, 162.5 mmol) added to each. Once dissolved, A and B were cooled to -10-C, C, D, and E were left at RT. DIC (25.4 ml, 162.5 mmol) was added in 5 ml portions over 1 hr to each bottle. Once the addition of DIC was complete, 3 bags were added to each bottle, and the solutions shaken overnight at RT. The bags were then removed from the anhydride solutions and washed 3X with DCM, 3X with MeOH and dried to yield the carboxynitrile attached to the resin through a carboxamide linkage. Kaiser test of the resins was negative.

List of Cyano Carboxylic Acids.

Resin A Cyanoacetic acid:13.8 g, 162.5 mmol

Resin B 1-Cyano-1-cyclopropane carboxylic acid: 18.1 g, 162.5 mmol

Resin C 3-Cyanobenzoic acid: 23.9 g, 162.5 mmol

Resin D 4-Cyanobenzoic acid: 23.9 g, 162.5 mmol

Resin E 2-(4-Cyanophenoxy)-2-methyl propionic acid: 33.3 g, 162.5 mmol

EXAMPLE 4

Preparation of DAB resin bound amines
by reductive amination
(Type 1 amines)

A 200 mg portion of DAB resin in a teabag was swollen in DMF + 1% AcOH. The amine or amine salt was added (0.25M amine) and the solutions shaken at RT for 1 hour. Sodium cyanoborohydride was then added (0.25 M) and the solution shaken at RT overnight. The supernatant was poured off and the resin washed with DMF (4X), MeOH (4X) and DCM (2X) to yield secondary amines on resin.

List of amines:

Isobutylamine
Benzylamine
Glycine t-butyl ester hydrochloride
1-(3-aminopropyl) imidazole

EXAMPLE 5

Preparation of Wang resin bound diamines (Type 2 amines)

Wang resin (100 g, 120 mmol) was swollen in DCM for 15 min and the excess poured off. A solution of carbonyl diimidazole (100 g, 0.5 mol) in 800 ml DCM was added and shaken for 3 hours. The solvent was poured off and the resin washed with DCM (2X) then a solution of anhydrous piperazine (43 g, 0.5 mol) in 800 ml DCM was added, and the solution shaken overnight. The supernatant was removed, and the resin washed with DCM, IPA, DMF, IPA and MeOH to yield piperazine linked to resin. The same procedure is followed with the following diamines:

1,10-diaminodecane
1,11-diaminoundecane

1,12-diaminododecane
1,2-diaminocyclohexane
1,3-bis(aminomethyl)cyclohexane
1,3-diamino-2-propanol
1,3-diaminopropane
1,4-diaminobutane
1,5-diamino-3-oxapentane
1,5-diaminopentane
1,6-hexanediamine
1,7-diaminoheptane
1,8-diaminooctane
1,9-diaminononane
2,2-dimethyl-1,3-propanediamine
2,2-dimethyl-1,5-diaminopentane
2-methyl-1,5-diaminopentane
2.4/2.6-diamino-1-methylcyclohexane mixture
3,3-oxetanebis(methylamine)dihydrobromide
4,4'-diaminodicyclohexylmethane
5-amino-2,2,4-trimethyl-1-cyclopentanemethylamine
9,9-bis(3-aminopropyl)fluorene
Trans-1,2-diaminocyclohexane
Trans-1,4-diaminocyclohexane

EXAMPLE 6

Acylation of resin bound amines with Cyanocarboxylic acids

To a solution of 4-cyanobenzoic acid (27 mmol, 4.0g) in 45 ml DCM/DMF (2:1) was added DIC (2.11 ml, 13.5 mmol). The solution was shaken 10 min, then DIEA (2.34 ml, 13.5 mmol) and DMAP (1.0 mmol, 120 mg) were added. The teabags containing resin-bound amines from Examples 4 and 5 were then added and the solution shaken overnight. The bags were washed with DCM, DMF, DCM and MeOH, then dried to yield 4-cyanobenzamide resin.

Other acids used:

Cyanoacetic acid
1-Cyano-1-cyclopropane carboxylic acid
3-Cyanobenzoic acid
2-(4-Cyanophenoxy)-2-methyl propionic acid

EXAMPLE 7
Acylation of resin bound amines with halocarboxylic acids

A teabag containing 100 g of resin bound piperazine from Examples 5 (120 mmol) was swollen in DCM and a solution of chloroacetic anhydride (41 g, 240 mmol) in 500 ml DCM was added, followed by DIEA (42 ml, 240 mmol). The solution was shaken at RT overnight, and washed with DCM, DMF, IPA and MeOH and dried to yield 4-chloroacetyl piperazine bound resin. Other primary and secondary amines of Example 4 and 5 are also used.

The halo carboxylic acids shown below can be substituted for chloroacetic anhydride and used in a similar manner, such as, preparing the anhydride of the carboxylic acid with diisopropyl carbodiimide in DCM for 30 minutes before addition of the amine resin.

4-(bromomethyl)benzoic acid
4-(chloromethyl)benzoic acid
Bromopyruvic acid
11-bromoundecanoic acid
12-bromododecanoic acid
3-bromopropionic acid
3-chloropropionic acid
3-iodopropionic acid
4-bromobutyric acid
4-chlorobutyric acid
3-chloropivalic acid
2-(bromomethyl)acrylic acid
5-bromovaleric acid

5-chlorovaleric acid
6-bromohexanoic acid
8-bromooctanoic acid
4-(bromomethyl)phenylacetic acid
4-(2-chloroethyl)benzoic acid
4-iodobutyric acid
6-iodohexanoic acid
4-(2-bromoethyl)-benzoic acid
7-bromoheptanoic acid
Bromopivalic acid
3-(chloromethyl)benzoic acid
4-(bromomethyl)-3-nitrobenzoic acid
4-(2-chloroacetamido)benzoic acid
2-(2-chloroacetamido)-4-thiazoleacetic acid

EXAMPLE 8

Alkylation of resin bound amines with cyanobenzyl bromides

A teabag containing 300 g of resin bound amine from Examples 4 and 5 (360 mmol) was swollen in DMF (1.5l) and 4-cyanobenzyl bromide (200g, 1.02 mmol) was added, followed by DIEA (177 ml, 1.02 mol). The solution was shaken at RT overnight and then washed with DCM, IPA and MeOH. The resin was dried under high vacuum to provide N-(4-cyano)benzylamine bound resin.

3-Cyanobenzyl bromide was used under the same conditions.

EXAMPLE 9

Coupling of Cyanophenols to Wang bromide resin

Wang bromide resin (70 g, 70 mmol) was washed with Dimethylacetamide (DMA). 4-cyanophenol (25g, 210 mmol) was dissolved in 500 ml DMA, and KOtBu (23.5 g, 210 mmol) was added in portions. The solution of phenolate

was added in one portion to the swollen resin and heated to 50-C overnight. The mixture was cooled and the resin was washed with DMF/H2O (4:1), DMF and MeOH 4 times each. The resin was then dried under vacuum to give 4-cyanophenol bound to resin via an ether linkage.

The following phenols were used in the same conditions:

4-hydroxy-3-methoxybenzonitrile
4-cyanophenol
2-fluoro-4-hydroxybenzonitrile
3-cyanophenol
4-cyano-4'-hydroxybiphenyl
2-cyanophenol
3,5-dibromo-4-hydroxybenzonitrile
4-hydroxybenzyl cyanide
3,5-diiodo-4-hydroxybenzonitrile
3,4-dihydroxybenzonitrile
4-hydroxytetrafluorobenzonitrile
3-bromo-4-hydroxybenzonitrile
3,5-di-tert-butyl-4-hydroxybenzonitrile
3,5-di-tert-butyl-4-hydroxyphenylacetonitrile
4-hydroxy-3-methoxyphenylacetonitrile
4-hydroxy-3-nitrobenzonitrile
3,5-dihydroxybenzonitrile
3-(4-hydroxyphenyl)propionitrile
3-ethoxy-4-hydroxyphenylacetonitrile
2-chloro-4-hydroxybenzonitrile
4-cyano-2-fluorophenol
3,5-dimethyl-4-hydroxybenzonitrile
2,6-dimethyl-4-hydroxybenzonitrile
2,6-dichloro-4-hydroxybenzonitrile
2-hydroxy-3-methoxyphenylacetonitrile
8-hydroxyquinoline-2-carbonitrile
3-hydroxy-naphthalene-2-carboxylic acid (3-cyano-phenyl)-amide

2-hydroxy-3-naphthoic acid-4-cyanoanilide
5-hydroxyindole-3-acetonitrile
3,4-dihydroxyphenylacetonitrile
Benzo(beta)-thiophene, 2-cyanomethyl-5-hydroxy-
3-chloro-4-hydroxybenzyl cyanide
4-chloro-2-hydroxybenzonitrile
2-cyano-6-nitro-phenol
2-hydroxy-5-nitrobenzonitrile
2-amino-4-cyanophenol
Methyl-2-hydroxy-5-cyano-benzoate
3-bromo-4-hydroxy-5-methoxy-phenylacetonitrile
3,5-dimethoxy-4-hydroxyphenyl-acetonitrile
4-cyano-2-iodo-6-nitrophenol

EXAMPLE 10

Coupling of Cyanophenols to Alkyl halides on resin

The chloroacetyl piperazine carbamate resin from Example 7 (330 g, 360 mmol) was swollen in DMA. To a solution of 4-cyanophenol (128.6 g, 1.08 mol) in 2 l DMA was added potassium t-butoxide (121.2 g, 1.08 mol) in portions. The solution was added to the resin bound alkyl halide, and the solution shaken at RT overnight. The resin was washed 3 times each with DMF, 5% H2O/DMF, 10% H2O/DMF, 20% H2O/DMF, IPA, and MeOH. The resin was then vacuum dried overnight to yield 4-cyanophenoxyacetylpiperazine carbamate resin.

The cyanophenols of Example 9 are also used in this step by substituting for 4-cyanophenol in the above procedure.

EXAMPLE 11

Coupling of BOC-cyanoethylglycine to MBHA

MBHA-HCl resin (5.0g, 4.05 mmol) was neutralized with 10% DIEA in DMF, then washed with DCM. N-BOC-N-cyanoethylglycine (2.05g, 9 mmol) and DIEA (1.56ml) were dissolved in 35 ml DCM, to which was added DIC (4.5 mmol, 0.71 ml). After 10 minutes HOBT (2.0 mmol, 0.3g) was added and the solution added to the resin. The solution was shaken overnight and then the resin was washed with DCM, DMF, MeOH, and dried in vacuo to give N-Boc cyanoethyl glycinamide linked to resin.

EXAMPLE 12

Synthesis of Amidoximes from Nitriles

General procedure:

Resin bound nitrile compounds prepared in examples 6,7,8,9,10, and 11 above were placed in teabags. Hydroxylamine-HCl (4-10 eq. based on loading of resin) and DIEA (4-10 eq) were placed in sufficient 2-methoxyethanol to give a 0.2 M solution. The resin was added and the solution heated to 80-85-C overnight. The solution was cooled to RT and the resin washed 4X with MeOH and dried to yield in each case the desired amidoxime bound to resin.

EXAMPLE 13

Synthesis of Library TRG 3600

Each of the nitrile resins from Example 3 was distributed to 36 bags with 400 mg of resin each according to Table 1: Distribution of Nitrile Resins and a number of control bags were made. To each of 36 tubes was added 55 ml of anhydrous 2-methoxyethanol, 0.83 g (12mmol) of Hydroxylamine Hydrochloride and 2.08 ml (12

mmol) DIEA. Once all the solids were dissolved the bags containing nitrile resins A-E were added (see table below) and the reaction tubes were heated to 85-C overnight. The tubes were cooled and the bags washed with MeOH (4X) and dried to yield the corresponding amidoxime.

List of Cyano Carboxylic Acids.

Resin A Cyanoacetic acid:13.8 g, 162.5 mmol

Resin B 1-Cyano-1-cyclopropane carboxylic acid: 18.1 g, 162.5 mmol

Resin C 3-Cyanobenzoic acid: 23.9 g, 162.5 mmol

Resin D 4-Cyanobenzoic acid: 23.9 g, 162.5 mmol

Resin E 2-(4-Cyanophenoxy)-2-methyl propionic acid: 33.3 g, 162.5 mmol

Table 1: Distribution of Nitrile Resins

Tube #	Bag #	Resin (g)	Excess NH2OH
1	A1, B1, C1, D1, E1	1.75	6.1
2	A3, B3, C3, D3, E3	1.75	6.1
3	A5, B5, C5, D5, E5	1.75	6.1
4	A7, B7, C7, D7, E7	1.75	6.1
5	A9, B9, C9, D9, E9	1.75	6.1
6	A11, B11, C11, D11, E11	1.75	6.1
7	A13, B13, C13, D13, E13	1.75	6.1
8	A15, B15, C15, D15, E15	1.75	6.1
9	A17, B17, C17, D17, E17	1.75	6.1
10	A19, B19, C19, D19, E19	1.75	6.1
11	A21, B21, C21, D21, E21	1.75	6.1

12	A23, B23, C23, D23, E23	1.75	6.1
13	A25, B25, C25, D25, E25	1.75	6.1
14	A27, B27, C27, D27, E27	1.75	6.1
15	A29, B29, C29, D29, E29	1.75	6.1
16	A31, B31, C31, D31, E31	1.75	6.1
17	A33, B33, C33, D33, E33	1.75	6.1
18	A35, B35, C35, D35, E35	1.75	6.1
19	A37, B37, C37, D37, E37	1.75	6.1
20	A39, B39, C39, D39, E39	1.75	6.1
21	A41, B41, C41, D41, E41	1.75	6.1
22	A43, B43, C43, D43, E43	1.75	6.1
23	A45, B45, C45, D45, E45	1.75	6.1
24	A47, B47, C47, D47, E47	1.75	6.1
25	A49, B49, C49, D49, E49	1.75	6.1
26	A51, B51, C51, D51, E51	1.75	6.1
27	A53, B53, C53, D53, E53	1.75	6.1
28	A55, B55, C55, D55, E55	1.75	6.1
29	A57, B57, C57, D57, E57	1.75	6.1
30	A59, B59, C59, D59, E59	1.75	6.1
31	A61, B61, C61, D61, E61	1.75	6.1
32	A63, B63, C63, D63, E63	1.75	6.1
33	A65, B65, C65, D65, E65	1.75	6.1
34	A67, B67, C67, D67, E67	1.75	6.1
35	A69, B69, C69, D69, E69	1.75	6.1
36	A71, B71, C71, D71, E71	1.75	6.1

EXAMPLE 14

Synthesis of Oxadiazoles from Amidoximes

General Procedure

A resin bound amidoxime of Example 12 was swollen in 2-methoxyethyl ether. A solution of the appropriate carboxylic acid anhydride (7 eq) in 2-methoxyethyl ether (0.2M) was added to the amidoxime. When the anhydride was not commercially available it was prepared from a solution of carboxylic acid (14 eq, 0.4M) in 2-methoxyethyl ether to which was added DIC (7 eq, 0.2M) and shaken for 30 minutes before addition of the resin bags. The solution of anhydride and the resin bound amidoxime were heated to 60-C for 16 hours. The solution was cooled and the resin washed twice with fresh 2-methoxyethyl ether. Sufficient 2-methoxyethyl ether was added to cover the resin and the solution heated to 85-C for 6 hours. The solvent was removed and the resin washed with DMF, DCM, MeOH and dried to give the anticipated oxadiazole bound resin.

EXAMPLE 15

Oxadiazoles from Amidoximes and BOC-Amino Acid Anhydrides TRG3600

To each of 36 tubes was added Boc-protected amino acid derivatives according to Table 2: Distribution of Amino Acids. Each amino acid (28 mmol) was dissolved in 55 ml of 2-methoxyethyl ether. To each tube was then added DIC (14 mmol) and the solution stirred at RT for 1 hr at which time a white precipitate had formed. The appropriate bags containing amidoxime from the previous step were then added and the reaction tubes were placed in a heating block at 60-C for 16 hr. The supernatant was removed and the resins washed twice with fresh 2-methoxyethyl ether. The bags were placed in 50 ml 2-

methoxyethyl ether and heated to 85-C for 6 hr. The tubes were cooled, and the bags washed 3X DMF, 3X DCM, 3X MeOH and dried to give 5-(N-Boc-amino)substituted oxadiazoles bound to resin.

Table 2: Distribution of Amino Acids

Tube #	Amino Acid	Mmol	Amt. (g)	Bag #
1	Boc-Alanine-OH	0.028	5.298	A1, B1, C1, D1, E1
2	Boc-b-Alanine-OH	0.028	5.298	A3, B3, C3, D3, E3
3	Boc-3-(Pyridyl)-Alanine-OH	0.028	7.484	A5, B5, C5, D5, E5
4	Boc-2-(Thienyl)-Alanine-OH	0.028	7.594	A7, B7, C7, D7, E7
5	Boc-a-Aminobutyric Acid-OH	0.028	5.692	A9, B9, C9, D9, E9
6	Boc-g-Aminobutyric Acid-OH	0.028	5.692	A11, B11, C11, D11, E11
7	Boc-e-Aminocaproic Acid-OH	0.028	6.476	A13, B13, C13, D13, E13
8	Boc-a-Aminoisobutyric Acid-OH	0.028	5.692	A15, B15, C15, D15, E15
9	Boc-trans-4-(Aminomethyl)-Cylohexane Carboxylic Acid-OH	0.028	7.202	A17, B17, C17, D17, E17
10	Boc-Arginine(Tos)-OH	0.028	11.998	A19, B19, C19, D19, E19
11	Boc-Aspartic Acid-OBzl	0.028	9.055	A21, B21, C21, D21, E21
12	Boc-Aspartic Acid(OcHex)-OH	0.028	8.831	A23, B23, C23, D23, E23

13	Boc-3-Carboxymethyl-1-Phenyl-1,3,8-triazaspiro[4.5]-decane-4-one-OH	0.028	10.905	A25, B25, C25, D25, E25
14	Boc-4-Chlorophenyl-alanine-OH	0.028	8.392	A27, B27, C27, D27, E27
15	Boc-Cyclohexyl-alanine-OH	0.028	7.599	A29, B29, C29, D29, E29
16	Boc-Glutamic Acid-OBzl	0.028	9.447	A31, B31, C31, D31, E31
17	Boc-Glutamic Acid(OcHex)-OH	0.028	9.223	A33, B33, C33, D33, E33
18	Boc-Glycine-OH	0.028	4.906	A35, B35, C35, D35, E35
19	Boc-Histidine(Tos)-OH	0.028	11.466	A37, B37, C37, D37, E37
20	Boc-Isoleucine-OH Hemihydrate	0.028	6.728	A39, B39, C39, D39, E39
21	Boc-Isonipecotic Acid-OH	0.028	6.418	A41, B41, C41, D41, E41
22	Boc-Leucine-OH Hydrate	0.028'	6.980	A43, B43, C43, D43, E43
23	Boc-Nipecotic Acid-OH	0.028	6.418	A45, B45, C45, D45, E45
24	Boc-Norleucine-OH	0.028	6.476	A47, B47, C47, D47, E47
25	Boc-Phenylalanine-OH	0.028	7.428	A49, B49, C49, D49, E49
26	Boc-D,L-Pipecolinic Acid-OH	0.028	6.418	A51, B51, C51, D51, E51
27	Boc-Proline-OH	0.028	6.028	A53, B53, C53, D53, E53
28	Boc-Serine(Bzl)-OH	0.028	8.268	A55, B55, C55, D55, E55

29	Boc-Thioproline-OH	0.028	6.530	A57, B57, C57, D57, E57
30	Boc-Threonine(Bzl)-OH	0.028	8.663	A59, B59, C59, D59, E59
31	Boc-TIC-OH	0.028	7.764	A61, B61, C61, D61, E61
32	Boc-Tryptophan(For)-OH	0.028	9.307	A63, B63, C63, D63, E63
33	Boc-Tyrosine(Bzl)-OH	0.028	10.399	A65, B65, C65, D65, E65
34	Boc-OEt-Tyrosine-OH	0.028	8.660	A67, B67, C67, D67, E67
35	Boc-Valine-OH	0.028	6.084	A69, B69, C69, D69, E69
36	N-Fmoc-Lysine(Boc)-OH	0.028	13.121	A71, B71, C71, D71, E71

EXAMPLE 16

Oxadiazoles from Amidoximes and FMOC-Amino Acid Anhydrides

The resin bound amidoximes from Example 12 were swollen in 2-methoxyethyl ether (0.1 mmol). The appropriate FMOC amino acids, Table 3: FMOC-amino acids, (3 mmol) were dissolved in 8 ml of 2-methoxyethyl ether. To each tube was then added DIC (1.5 mmol) and the solution stirred at RT for 1 hr at which time a white precipitate had formed. The appropriate bags containing amidoxime were then added and the reaction tubes were placed in a heating block at 60-C for 16 hr. The supernatant was removed and the resins washed twice with fresh 2-methoxyethyl ether. The bags were placed in 10 ml 2-methoxyethyl ether and heated to 85-C for 6 hr. The tubes were cooled, and the bags washed 3X DMF, 3X DCM, 3X MeOH and dried to give 5-((N-FMOC-amino)substituted oxadiazoles bound to resin.

Table 3 FMOC-amino acids

NO.	FMOC-Amino Acid
1	FMOC-phenylalanine
2	FMOC-b-alanine
3	FMOC-arginine-(PMC)-OH
4	FMOC-arginine-(TOS)-OH
5	FMOC-isonipecotic acid
6	FMOC-L-proline
7	FMOC-L-valine
8	FMOC-L-isoleucine
9	FMOC-L-tryptophan
10	FMOC-ser(TBU)-OH
11	FMOC-L-phenylalanine
12	FMOC-tyr(TBU)-OH
13	FMOC-cys(TBU)-OH
14	FMOC-asp(OTBU)-OH
15	FMOC-L-asparagine
16	FMOC-L-leucine
17	FMOC-L-methionine
18	FMOC-glu(OTBU)-OH
19	N-ALPHA-FMOC-L-glutamine
20	FMOC-lys(BOC)-OH
21	FMOC-L-alanine
22	FMOC-gly-OH
23	FMOC-nle-OH
24	FMOC-cys(TRT)-OH
25	FMOC-cys(ACM)-OH
26	FMOC-cys(STBU)-OH
27	FMOC-arg(MTR)-OH
28	FMOC-his(TRT)-OH
29	FMOC-p-nitro-phe-OH
30	BOC-lys(FMOC)-OH

31	FMOC-D-val-OH
32	FMOC-D-trp-OH
33	FMOC-D-phe-OH
34	FMOC-D-asn-OH
35	FMOC-D-leu-OH
36	FMOC-D-met-OH
37	FMOC-D-gln-OH
38	FMOC-D-ala-OH
39	FMOC-BETA-ala-OH
40	N-FMOC-3,5-diiodo-L-tyrosine
41	FMOC-arg(TOS)-OH
42	FMOC-cha-OH
43	FMOC-D-arg(MTR)-OH
44	FMOC-arg(NO_2)-OH
45	FMOC-arg(PMC)-OH
46	FMOC-D-arg(PMC)-OH
47	FMOC-D-arg(TOS)-OH
48	FMOC-asn(MBH)-OH
49	FMOC-D-asn(MBH)-OH
50	FMOC-asp(O-2-ADA)-OH
51	FMOC-asp(OBzl)-OH
52	FMOC-asp-OTBU
53	FMOC-cys(BZL)-OH
54	FMOC-cys(PMEOBZL)-OH
55	FMOC-glu(OBzl)-OH
56	FMOC-gln(MBH)-OH
57	FMOC-D-gln(MBH)-OH
58	FMOC-glu-OTBU
59	FMOC-L-ALPHA-T-butylglycine
60	FMOC-TBU-D-gly-OH
61	FMOC-hyp-OH
62	FMOC-hyp(TBU)-OH

63	FMOC-D-lys(BOC)-OH
64	FMOC-lys(Z)-OH
65	FMOC-D-lys(Z)-OH
66	FMOC-lys(2-CL-Z)-OH
67	FMOC-orn(BOC)-OH
68	FMOC-ser(BZL)-OH
69	FMOC-sta-OH
70	FMOC-thi-OH
71	FMOC-D-thi-OH
72	FMOC-tyr(2-BR-Z)-OH
73	FMOC-D-tyr(TBU)-OH
74	FMOC-tyr(2,6-dichloro-BZL)-OH
75	FMOC-EPSILON-acp-OH
76	FMOC-asn(TRT)-OH
77	FMOC-D-asp(OTBU)-OH
78	FMOC-D-cys(ACM)-OH
79	FMOC-D-glu(OTBU)-OH
80	FMOC-gln(TRT)-OH
81	N-ALPHA-FMOC-pI-benzyloxymethyl-L-histidine
82	FMOC-D-his(TRT)-OH
83	FMOC-met(O)-OH
84	FMOC-D-orn(BOC)-OH
85	FMOC-D-phe(4-cl)-OH
86	FMOC-D-pro-OH
87	FMOC-D-ser-OH
88	FMOC-D-ser(TBU)-OH
89	FMOC-thr-OH
90	FMOC-thr(BZL)-OH
91	FMOC-thr(TBU)-OH
92	FMOC-asp(O-1-ADA)-OH
93	FMOC-lys(AC)-OH
94	FMOC-abu-OH

95	FMOC-lys(FMOC)-OH
96	N-FMOC-4-chloro-L-phenylalanine
97	FMOC-D-thr(TBU)-OH
98	FMOC-tyr-OH
99	FMOC-D-tic-OH
100	FMOC-tic-OH
101	FMOC-GAMMA-abu-OH
102	FMOC-D-cha-OH
103	FMOC-aib-OH
104	FMOC-D-asn(TRT)-OH
105	FMOC-D-cys(TRT)-OH
106	FMOC-N-ME-gly-OH
107	FMOC-ME-leu-OH
108	FMOC-D-pen(ACM)-OH
109	FMOC-pen(ACM)-OH
110	FMOC-ME-phe-OH
111	FMOC-DELTA-pro-OH
112	FMOC-cit-OH
113	FMOC-arg(MTS)-OH
114	FMOC-L-asn(TMOB)-OH
115	FMOC-L-gln(TMOB)-OH
116	FMOC-D-gln(TRT)-OH
117	FMOC-his(BOC)-OH
118	FMOC-his(MTT)-OH
119	FMOC-lys(TFA)-OH
120	FMOC-met(O_2)-OH
121	FMOC-orn(FMOC)-OH
122	FMOC-ser(TRT)-OH
123	FMOC-D-thr
124	FMOC-trp(BOC)-OH
125	FMOC-D-trp(BOC)-OH
126	FMOC-ME-ala-OH

127	FMOC-D-ME-ala-OH
128	FMOC-ME-ile-OH
129	FMOC-D-ME-phe-OH
130	FMOC-ME-val-OH
131	FMOC-D-ME-val-OH
132	FMOC-AHPPA
133	FMOC-nva-OH
134	FMOC-phg-OH
135	FMOC-D-nle-OH
136	FMOC-D-nva-OH
137	FMOC-D-phg-OH
138	FMOC-L-arg-(PBF)-OH
139	FMOC-D-arg(PBF)-OH
140	FMOC-D-asp-OTBU
141	FMOC-thr(TRT)-OH
142	FMOC-lys(MTT)-OH
143	FMOC-cys(MMT)-OH
144	FMOC-hse(TRT)-OH
145	FMOC-L-pentafluorophenylalanine
146	FMOC-lys(DDE)-OH
147	DDE-lys(FMOC)-OH
148	FMOC-asp-OAII
149	FMOC-D-dpr(DDE)-OH
150	FMOC-L-dpr(DDE)-OH
151	FMOC-glu-OALL
152	FMOC-ser[PO(OH)-OBzl]-OH
153	FMOC-his(TOS)
154	FMOC-tyr(ME)-OH
155	FMOC-ACHPA
156	FMOC-orn(MTT)-OH
157	FMOC-asu-OME
158	FMOC-glu(ODMAB)-OH

159	FMOC-D-his(BOC)-OH
160	FMOC-glu-ODMAB
161	FMOC-APNS
162	FMOC-asp(ODMAB)-OH
163	FMOC-(FMOCHMB)asp(OTBU)-OH
164	FMOC-D-orn(MTT)-OH
165	FMOC-(FMOCHMB)lys(BOC)-OH
166	FMOC-thr(PO(OBzl)OH)-OH
167	FMOC-tyr(PO(OBzl)OH)-OH

EXAMPLE 17

5-Chloromethyl Oxadiazoles from Amidoximes

To a solution of chloroacetic anhydride (0.2M) in 2-Methoxyethyl ether (8 eq.) was added teabags containing Amidoximes from Example 12 . The reaction tubes were placed in a heating block at 60-C for 16 hrs, the supernatant removed and the resins washed twice with fresh 2-methoxyethyl ether. The bags were covered in 2-methoxyethyl ether and heated to 85-C for 6 hr. The tubes were cooled, and the bags washed 3X times each with DMF, DCM, MeOH and dried to give 5-chloromethyl oxadiazoles bound to resin.

EXAMPLE 18

5-Aminomethyl oxadiazoles from 5-Chloromethyl Oxadiazoles

The resins from Example 17 were placed in a solution of amine according to Table 3: Primary and secondary amines (0.2 M, 10 eq) in anhydrous DMF and shaken at RT for 2 hrs. The bags were then washed with DMF 4X, DCM 2X and MeOH to give 5-substituted aminomethyl oxadiazoles bound to resin.

Table 4: Primary and secondary amines

1	1-(2-Aminoethyl)pyrrolidine
2	2-(Aminomethyl)pyridine
3	Histamine
4	Cyclopentylamine
5	Allylamine
6	2-Methoxyethylamine
7	(+/-)-Tetrahydrofurylamine
8	Benzylamine
9	2-Methylbenzylamine
10	3-Methylbenzylamine
11	4-Methylbenzylamine
12	2-Fluorobenzylamine
13	3-Fluorobenzylamine
14	4-Fluorobenzylamine
15	1-(3-Aminopropyl)imidazole
16	p-Xylylenediamine,
17	4-Methoxybenzylamine
18	3-Chlorobenzylamine
19	3-Bromobenzylamine HCl
20	4-Bromobenzylamine HCl
21	Cyclopropylamine
22	(Aminomethyl)cyclopropane
23	4-(Aminomethyl)pyridine
24	3-(Aminomethyl)pyridine
25	2-Thiophenemethylamine
26	Phenethylamine
27	4-(2-Aminoethyl)morpholine
28	3-Methoxybenzylamine
29	Piperonylamine
30	4-Methoxyphenethylamine
31	2-Fluorophenethylamine
32	2-(4-Chlorophenyl)ethylamine

33	2-(3-Chlorophenyl)ethylamine
34	2-(2-Chlorophenyl)ethylamine
35	2,3-Dimethoxybenzylamine
36	3,4-Dimethoxyphenethylamine
37	2,4-Dichlorophenethylamine
38	N,N-Diethylethylenediamine
39	2-(2-Aminoethyl)-1-methylpyrrolidine
40	3-Diethylaminopropylamine
41	2-(2-Aminoethylamino)-5-nitropyridine
42	N,N,2,2-Tetramethyl-1,3-propanediamine
43	3-Dimethylaminopropylamine
44	Ethylenediamine
45	1-(2-Aminoethyl)piperidine
46	isoamylamine
47	3-Ethoxypropylamine
48	1-(3-Aminopropyl)-2-pipecoline
49	3-Butoxypropylamine
50	N-(3'-Aminopropyl)-2-pyrrolidinone, tech
51	4-(3-Aminopropyl)morpholine
52	N-(2-Aminoethyl)-N-ethyl-m-toluidine
53	3-Phenyl-1-propylamine
54	b-Methylphenethylamine
55	4-Phenylbutylamine
56	3,3-Diphenylpropylamine
57	Isobutylamine
58	2-(2-Aminoethyl)pyridine
59	Cyclohexanemethylamine
60	3-Methoxyphenethylamine
61	3-Phenylbenzylamine
62	Piperazine

EXAMPLE 19

Acylation of Oxadiazole Amines - General procedure

The Boc-protected Oxadiazole resins of Example 15 were treated with two portions of 50% TFA/DCM (5 min. then 30 min.), washed 3 times each with DCM, MeOH, MTBE and dried. The FMOC-protected Oxadiazole resins of Example 16 were treated with two portions of 20% piperidine in DMF, then washed with DMF, MeOH, MTBE and dried. The aminomethyl oxadiazoles of Example 18 were used without further precautions. The resins were suspended in DMF and distributed into a 96 well microtiter plate. The supernatant solvent was removed and the following solutions were added: a carboxylic acid solution, a solution of DMAP, HOBT and DIEA, a solution of DIC in DMF or DCM. Other coupling agents such as BOP, PyBOP, HATU, HBTU and others known in the art were also used in separate experiments. The quantities of each solution were adjusted according to the amount of resin per well in the plate, in order to have a five to tenfold excess of reagents. The 96 well plates were capped and shaken overnight at RT. The resins were then washed with DMF (8X), MeOH (4X) and the resin allowed to dry resulting in the N-acylated-5-(substituted aminomethyl)oxadiazoles bound to resin.

List of Carboxylic acids

No.	Carboxylic Acid	Group
1	(3,4-Dimethoxyphenyl)Acetic acid	1
2	(a,a,a-Trifluoro-m-Tolyl)acetic acid	1
3	(Methylthio)acetic acid	1
4	1-(4-Chlorophenyl)-1-Cyclopentanecarboxylic acid	1
5	1-Adamantaneacetic acid	1
6	1-cyano-1-cyclopropane carboxylic acid	1
7	1-Naphthylacetic acid	1

8	1-Phenyl-1-Cyclopropanecarboxylic acid	1
9	2,4-Dichlorobenzoic acid	1
10	2-(2-cyanophenylthio)benzoic acid	1
11	2-(methylthio)nicotinic acid	1
12	2-chloro-5-(methylthio)benzoic acid	1
13	2-Fluorobenzoic acid	1
14	2-Methylcyclopropanecarboxylic acid	1
15	2-Norbornaneacetic acid	1
16	2-Pyrazinecarboxylic acid	1
17	2-Thiopheneacetic acid	1
18	3,4,5-Trimethoxyphenylacetic acid	1
19	3,4-Dichlorobenzoic acid	1
20	3,4-Dichlorophenylacetic acid	1
21	3,5,5-Trimethylhexanoic acid	1
22	3,5-Di-tert-butyl-4-hydroxybenzoic acid	1
23	3,5-Dichloro-4-hydroxybenzoic acid	1
24	3-Benzoylpropionic acid	1
25	3-Bromo-4-Methylbenzoic acid	1
26	3-Cyanobenzoic acid	1
27	3-Fluoro-4-Methylbenzoic acid	1
28	3-Indolepropionic acid	1
29	3-Methyl-2-thiophenecarboxaldehyde	1
30	3-Phenoxybenzoic acid	1
31	4-(dimethylamino)butyric acid hydrochloride	1
32	4-(methylthio)benzoic acid	1
33	4-Biphenylacetic acid	1
34	4-Bromophenylacetic acid	1
35	4-carboxybenzenesulfonamide	1
36	4-Cyanobenzoic acid	1
37	4-Dimethylaminobenzoic acid	1
38	4-Ethoxyphenylacetic acid	1
39	4-Fluorophenylacetic acid	1
40	4-Iodobenzoic acid	1
41	4-Isopropoxybenzoic acid	1
42	4-Isopropylbenzoic acid	1
43	4-Methyl-1-Cyclohexanecarboxylic acid	1
44	4-Methylvaleric acid	1

	45	4-nitrophenylacetic acid	1
	46	4-Phenoxybenzoic acid	1
	47	4-tert-Butyl-cyclohexanecarboxylic acid	1
	48	5-Bromo-2-chlorobenzoic acid	1
	49	5-Bromonicotinic acid	1
	50	5-Methoxyindole-2-carboxylic acid	1
	51	5-Methylsalicylic acid	1
	52	6-Chloronicotinic acid	1
	53	Acetic acid	1
	54	alpha-Methylcinnamic acid	1
	55	Benzoic acid	1
	56	coumarin-3-carboxylic acid	1
	57	Crotonic acid	1
	58	Cyclohexanepropionic acid	1
	59	diphenylacetic acid	1
	60	DL-2-(3-Chlorophenoxy)-propionic acid	1
	61	Hydrocinnamic acid	1
	62	Isobutyric acid	1
	63	Isonicotinic acid	1
	64	Isovaleric acid	1
	65	Levulinic acid	1
	66	m-Anisic acid	1
	67	m-Toluic acid	1
	68	Methoxyacetic acid	1
	69	Nicotinic acid	1
	70	p-Tolylacetic acid	1
	71	Picolinic acid	1
	72	Piperonylic acid	1
	73	R(-)-2-oxothiazolidine-4-carboxylic acid	1
	74	S-(+)-Mandelic acid	1
	75	succinamic acid	1
	76	Tetrahydro-3-furoic acid	1
	77	theophylline-7-acetic acid	1
	78	trans-3-(3-Pyridyl)acrylic acid	1
	79	Trimethylacetic acid	1
	80	Triphenylacetic acid	1
	81	(+/-)-camphorcarboxylic acid	2

	82	1-(4-chlorophenyl)-1-cyclohexanecarboxylic acid	2
	83	1-acetylpiperidine-4-carboxylic acid	2
	84	1-methyl-1-cyclohexanecarboxylic acid	2
	85	1-Phenyl-5-(trifluoromethyl)pyrazole-4-carboxylic acid	2
	86	2,2,3,3-tetramethylcyclopropanecarboxylic acid	2
	87	2,4-dibromophenoxyacetic acid	2
	88	2,5-dimethyl-3-furoic acid	2
	89	2,6-dichlorocinnamic acid	2
	90	2-(2,6-Dimethylmorpholino)-5-Nitrobenzoic acid	2
	91	2-(2-(2-methoxyethoxy)ethoxy)acetic acid	2
	92	2-(allylthio)nicotinic acid	2
	93	2-(carboxymethylthio)pyrimidine	2
	94	2-(pentamethylbenzoyl)benzoic acid	2
	95	2-bromo-5-methoxybenzoic acid	2
	96	2-chloro-n-butyric acid	2
	97	2-cyano-3-(4-methoxy-phenyl)-acrylic acid	2
	98	2-furoic acid	2
	99	2-hydroxyisobutyric acid	2
	100	2-methyl-3-butenoic acid	2
	101	2-methylvaleric acid	2
	102	2-phenoxynicotinic acid	2
	103	2-phenyl-4-quinolinecarboxylic acid	2
	104	3,3'-dichloropivalic acid	2
	105	3,3-diphenylpropionic acid	2
	106	3,4-difluorobenzoic acid	2
	107	3,4-dihydro-2,2-dimethyl-4-oxo-2h-pyran-6-carboxylic acid	2
	108	3,4-dimethoxybenzoic acid	2
	109	3,5-dibenzyloxybenzoic acid	2
	110	3,5-dimethylisoxazole-4-carboxylic acid	2
	111	3-(3-thienyl)acrylic acid	2
	112	3-Ethoxythiophene-2-carboxylic acid	2
	113	3-methoxycyclohexanecarboxylic acid	2

114	3-methoxypropionic acid	2
115	3-methyl-4-nitrobenzoic acid	2
116	3-pyridinepropionic acid	2
117	3-[4-(3,4-Dichlorobenzyloxy)phenyl]acrylic acid	2
118	4'-(trifluoromethyl)-2-biphenylcarboxylic acid	2
119	4-(1h-pyrrol-1-yl)benzoic acid	2
120	4-(3-methyl-5-oxo-2-pyrazolin-1-yl)benzoic acid	2
121	4-acetoxycinnamic acid	2
122	4-acetyl-3,5-dimethyl-2-pyrrolecarboxylic acid	2
123	4-acetylphenoxyacetic acid	2
124	4-azidobenzoic acid	2
125	4-benzyloxyphenoxyacetic acid	2
126	4-butoxyphenylacetic acid	2
127	4-Carboxy-1-(4-Chlorobenzyl)pyrrolidin-2-one	2
128	4-Carboxy-1-(furfuryl)pyrrolidin-2-one	2
129	4-Carboxy-1-(then-2-yl) pyrrolidin-2-one	2
130	4-cyclohexylbenzoic acid	2
131	4-guanidinobutyric acid	2
132	4-hydroxy-3-(morpholinomethyl)benzoic acid	2
133	4-iodophenoxyacetic acid	2
134	4-isopropylcinnamic acid	2
135	4-methoxy-2-quinolinecarboxylic acid	2
136	4-methoxycyclohexanecarboxylic acid	2
137	4-Methyl-1,2,3-thiadiazole-5-carboxylic acid	2
138	4-N-propylbenzoic acid	2
139	4-nitrobenzoic acid	2
140	4-pentylbenzoic acid	2
141	4-phenoxybutyric acid	2
142	4-thioureido-benzoic acid	2
143	5-(4-chlorophenyl)-2-furoic acid	2
144	5-methyl-3-phenylisoxazole-4-carboxylic acid	2
145	6-bromocoumarin-3-carboxylic acid	2

146	6-hydroxypicolinic acid	2
147	6-methylchromone-2-carboxylic acid	2
148	7-methoxy-2-benzofurancarboxylic acid	2
149	alpha-bromophenylacetic acid	2
150	alpha-cyanocinnamic acid	2
151	alpha-phenyl-o-toluic acid	2
152	alpha-phenylcinnamic acid	2
153	benzofuran-2-carboxylic acid	2
154	benzyloxyacetic acid	2
155	bicyclo(2.2.1)hept-5-ene-2-carboxylic acid	2
156	citrazinic acid	2
157	coumalic acid	2
158	cyclohexylidenecyanoacetic acid	2
159	cyclopentylacetic acid	2
160	cyclopropanecarboxylic acid	2
161	diethyl 1,3,5-benzenetricarboxylate	2
162	diethylphosphonoacetic acid	2
163	3-(2-chloro-6-fluorophenyl)-5-methylisoxazole-4-carboxylic acid	2
164	flurbiprofen	2
165	hydantoic acid	2
166	ibuprofen	2
167	itaconic acid monomethyl ester	2
168	L-pyroglutamic acid	2
169	Phenylmalonic acid monobenzyl ester	2
170	mesitylglyoxylic acid	2
171	monoethyl fumarate	2
172	N,N-dimethylglycine	2
173	N-(2,4-difluorophenyl)maleamic acid	2
174	N-(3-methoxyphenyl)maleamic acid	2
175	N-(4-carboxyphenyl)succinimide	2
176	N-(4-nitrobenzoyl)-beta-alanine	2
177	N-carbamoylmaleamic acid	2
178	N-carboxyethylrhodanine	2
179	N-phthaloylglycine	2
180	p-toluic acid	2
181	phthalide-3-acetic acid	2

	182	pinonic acid	2
	183	probenecid	2
	184	quinaldic acid	2
	185	thiazolidine-2-carboxylic acid	2
5	186	thymine-1-acetic acid	2
	187	trans-2-(2-methoxyphenyl)-5-oxotetrahydrofuran-3-carboxylic acid	2
	188	trans-2-phenyl-1-cyclopropanecarboxylic acid	2
	189	uracil-5-carboxylic acid monohydrate	2
10	190	(4-Pyridylthio)acetic acid	3
	191	1,3-phenylene diacetic acid	3
	192	1-Adamantanecarboxylic acid	3
	193	2-Acetylbenzoic acid	3
	194	2-Benzimidazolepropionic acid	3
15	195	2-Imino-1-imidazolidineacetic acid	3
	196	2-Methoxy-4-(methylthio)-benzoic acid	3
	197	2-Naphthylacetic acid	3
	198	2-Napthoic acid	3
	199	3,4-Dimethoxycinnamic acid	3
20	200	3,5-bis(Trifluoromethyl)benzoic acid	3
	201	3,5-Dichlorobenzoic acid	3
	202	3-Acetamidobenzoic acid	3
	203	3-Carboxy-1,4-dimethyl-2-pyrroleacetic acid	3
	204	3-Chloro-4-hydroxybenzoic acid hemihydrate	3
25	205	3-Hydroxyphenylacetic acid	3
	206	3-Indoleglyoxylic acid	3
	207	4'-Ethyl-4-biphenylcarboxylic acid	3
	208	4-Fluoro-alpha-methylphenylacetic acid	3
	209	4-Hydroxyquinoline-2-carboxylic acid hydrate	3
	210	4-Nitrophenyl guanidinobenzoate hydrochloride	3
	211	4-Pyridylacetic acid hydrochloride	3
	212	4-Sulfobenzoic acid, potassium salt	3
35	213	5-Benzimidiazolecarboxylic acid	3
	214	Benzotriazole-5-carboxylic acid	3
	215	Benzoylformic acid	3

216	Furylacrylic acid	3
217	Indole-6-carboxylic acid	3
218	N-Acetylanthranilic acid	3
219	Nalidixic acid	3
220	Niflumic acid	3
221	Oxolinic acid	3
222	Pyrrole-2-carboxylic acid	3
223	trans-3-Furanacrylic acid	3
224	Xanthene-9-carboxylic acid	3
225	(Phenylthio)acetic acid	4
226	1-Isoquinolinecarboxylic acid	4
227	2-Pyridylacetic acid hydrochloride	4
228	3,4,5-Triethoxybenzoic acid	4
229	3,4-(Methylenedioxy)-Phenylacetic acid	4
230	3,5-Bis(Trifluoromethyl)-Benzoic acid	4
231	3,5-Dimethyl-p-anisic acid	4
232	3-Thiopheneacetic acid	4
233	4-Ethoxybenzoic acid	4
234	4-Hydroxybenzoic acid	4
235	Boc-isonipecotic acid	4
236	Cyclobutanecarboxylic acid	4

EXAMPLE 20

Sulfonylation of Oxadiazole Amines

The Boc-protected oxadiazole resins of Example 15 were treated with two portions of 50% TFA/DCM (5 min. then 30 min.), washed 3 times each with DCM, MeOH, MTBE and dried. The FMOC-protected oxadiazole resins of Example 16 were treated with two portions of 20% piperidine in DMF, then washed with DMF, MeOH, MTBE and dried. The aminomethyl oxadiazoles of Example 18 were used without further precautions. The resins were suspended in DMF and distributed into a 96 well microtiter plate. The supernatant solvent was removed, and the resin washed with acetonitrile. A solution of N-methylimidazole (5.5 to 11 eq/mmol resin) in acetonitrile

was added followed by a solution of sulfonyl chloride in ACN (5 to 10 eq/mmol resin). The plates were capped and vortexed and shaken overnight. The plates were then washed with ACN (8X) and MeOH (8X), and dried to give substituted 5-(N-sulfonyl)-oxadiazoles bound to resin.

List of Sulfonyl chlorides.

(1r)-(-)-10-camphorsulfonyl chloride
1,2-naphthoquinone-2-diazido-4-sulfonyl chloride
1,2-naphthoquinone-2-diazido-4-sulfonyl chloride
1-butanesulfonyl chloride
1-naphthalenesulfonyl chloride
1-propanesulfonyl chloride
10-camphorsulfonyl chloride
2,2,2-trifluoroethanesulfonyl chloride
2,3,4-trichlorobenzenesulfonyl chloride
2,3,4-trifluorobenzenesulphonyl chloride
2,3,5,6-tetramethylbenzenesulfonyl chloride
2,3-dichlorobenzenesulfonyl chloride
2,3-dichlorothiophene-5-sulphonyl chloride
2,4,5-trichlorobenzenesulfonyl chloride
2,4,5-trifluorobenzenesulfonyl chloride
2,4,6-trichlorobenzenesulfonyl chloride
2,4,6-triisopropylbenzenesulfonyl chloride
2,4-dichlorobenzenesulfonyl chloride
2,4-difluorobenzenesulfonyl chloride
2,4-dinitrobenzenesulfonyl chloride
2,5-di(2,2,2-trifluoroethoxy)benzenesulphonyl chloride
2,5-dibromo-3,6-difluorobenzenesulfonyl chloride
2,5-dibromobenzenesulfonyl chloride
2,5-dichlorobenzenesulfonyl chloride
2,5-dichlorothiophene-3-sulphonyl chloride
2,5-dimethoxybenzenesulfonyl chloride
2,6-dichloro-4-(trifluoromethyl)benzenesulfonyl chloride
2,6-dichlorobenzenesulfonyl chloride
2,6-difluorobenzenesulfonyl chloride

2-(1-naphthyl)ethanesulfonyl chloride
2-(trifluoromethoxy)benzenesulfonyl chloride
2-(trifluoromethyl)benzenesulfonyl chloride
2-acetamido-4-methyl-5-thiazolesulfonyl chloride
2-bromobenzenesulfonyl chloride
2-chloro-4-(trifluoromethylbenzene)sulfonyl chloride
2-chloro-4-fluorobenzenesulfonyl chloride
2-chloro-5-(trifluoromethyl)benzenesulfonyl chloride
2-chloro-6-methylbenzenesulfonyl chloride
2-chlorobenzenesulfonyl chloride
2-chloroethanesulfonyl chloride
2-cyanobenzenesulfonyl chloride
2-fluorobenzenesulfonyl chloride
2-mesitylenesulfonyl chloride
2-methyl-5-nitrobenzenesulfonyl chloride
2-methylsulfonylbenzenesulfonyl chloride
2-naphthalenesulfonyl chloride
2-nitro-4-(trifluoromethyl)benzenesulfonyl chloride
2-nitro-alpha-toluenesulfonyl chloride
2-nitrobenzenesulfonyl chloride
2-thiophenesulfonyl chloride
2-[1-methyl-5-(trifluoromethyl)pyrazol-3-yl]-thiophene-5-sulfonyl chloride
2-[3-(trifluoromethyl)pyrid-2-ylsulfonyl]-thiophene-5-sulfonyl chloride
2-[5-(trifluoromethyl)pyrid-2-ylsulfonyl]-thiophene-5-sulfonyl chloride
3,4-dibromobenzenesulfonyl chloride
3,4-dichlorobenzenesulfonyl chloride
3,4-difluorobenzenesulphonyl chloride
3,4-dimethoxybenzenesulfonyl chloride
3,5-bis(trifluoromethyl)benzenesulfonyl chloride
3,5-dibromothiophene-2-sulfonyl chloride
3,5-dichloro-2-hydroxybenzenesulfonyl chloride
3,5-dichloro-4-hydroxybenzenesulphonyl chloride
3,5-dichlorobenzenesulfonyl chloride
3,5-dimethylisoxazole-4-sulfonyl chloride

3,5-dinitro-4-methoxybenzenesulfonyl chloride
3-(chlorosulfonyl)benzoic acid
3-(trifluoromethyl)benzenesulfonyl chloride
3-bromobenzenesulfonyl chloride
3-chloro-2-methylbenzenesulfonyl chloride
3-chloro-4-fluorobenzenesulfonyl chloride
3-chlorobenzenesulfonyl chloride
3-chloropropanesulfonyl chloride
3-fluorobenzenesulfonyl chloride
3-nitrobenzenesulfonyl chloride
4,5-dibromothiophene-2-sulfonyl chloride
4-(bromomethyl)benzenesulphonyl chloride
4-(chlorosulfonyl)benzoic acid
4-(chlorosulfonyl)phenyl isocyanate
4-(N-butoxy)benzenesulfonyl chloride
4-(trifluoromethoxy)benzenesulfonyl chloride
4-(trifluoromethyl)benzenesulfonyl chloride
4-acetamido-3-chlorobenzenesulfonyl chloride
4-acetamidobenzenesulfonyl chloride
4-benzenesulphonylthiophene-2-sulphonyl chloride
4-biphenylsulfonyl chloride
4-bromo-2,5-dichlorothiophene-3-sulfonyl chloride
4-bromo-2,5-difluorobenzenesulphonyl chloride
4-bromo-2-(trifluoromethoxy)benzene sulphonyl chloride
4-bromobenzenesulfonyl chloride
4-chloro-3-nitrobenzenesulfonyl chloride
4-chloro-7-chlorosulfonyl-2,1,3-benzoxadiazole
4-chlorobenzenesulfonyl chloride
4-cyanobenzenesulfonyl chloride
4-dimethylaminoazobenzene-4'-sulfonyl chloride
4-ethylbenzenesulfonyl chloride
4-fluorobenzenesulfonyl chloride
4-isopropylbenzenesulfonyl chloride
4-methoxy-2,3,6-trimethyl benzenesulfonyl chloride
4-methoxy-2,3,6-trimethylbenzoylsulfonyl chloride
4-methoxy-2,6-dimethylbenzenesulfonyl chloride
4-methoxy-2-nitrobenzenesulfonyl chloride

4-methoxybenzenesulfonyl chloride
4-methyl-3-nitrobenzenesulfonyl chloride
4-methylsulfonylbenzenesulfonyl chloride
4-N-amylbenzenesulfonyl chloride
4-N-amylbenzenesulfonyl chloride
4-N-butylbenzenesulfonyl chloride
4-N-propylbenzenesulfonyl chloride
4-N-propylbenzenesulfonyl chloride
4-nitrobenzenesulfonyl chloride
4-phenylazobenzenesulfonyl chloride
4-tert-butylbenzenesulfonyl chloride
5-bromo-2-methoxybenzenesulfonyl chloride
5-bromothiophene-2-sulfonyl chloride
5-chloro-2-methoxybenzenesulfonyl chloride
5-chloro-4-nitrothiophene-2-sulfonyl chloride
5-chloronaphthalene-1-sulfonyl chloride
5-chloronaphthalene-2-sulfonyl chloride
5-chlorothiophene-2-sulfonyl chloride
5-diethylamino-1-naphthalenesulfonyl chloride
5-fluoro-2-methylbenzenesulfonyl chloride
5-[3-chloro-5-(trifluoromethyl)pyrid-2-yl-sulfonyl]thiophene-2-sulfonyl chloride
6-methoxy-m-toluenesulfonyl chloride
8-quinolinesulfonyl chloride
9,10-dibromoanthracene-2-sulfonyl chloride
alpha-toluenesulfonyl chloride
bansyl chloride
benzenesulfonyl chloride
beta-styrene sulfonyl chloride
beta-styrene sulfonyl chloride
d-camphor-10-sulfonyl chloride
d-camphor-10-sulfonyl chloride
dansyl chloride
ethanesulfonyl chloride
isopropylsulfonyl chloride
isoquinoline-5-sulfonyl chloride
m-toluenesulfonyl chloride

methanesulfonyl chloride
methyl 2-(chlorosulfonyl)benzoate
O-toluenesulfonyl chloride
p-styrenesulfonyl chloride
p-toluenesulfonyl chloride
p-xylene-2-sulfonyl chloride
pentafluorobenzenesulfonyl chloride
pentamethylbenzenesulfonyl chloride
pipsyl chloride
pmc-cl

EXAMPLE 21

Synthesis of Oxadiazole Ureas

The Boc-protected oxadiazole resins of Example 15 were treated with two portions of 50% TFA/DCM (5 min. then 30 min.), washed 3 times each with DCM, MeOH, MTBE and dried. The FMOC-protected oxadiazole resins of Example 16 were treated with two portions of 20% piperidine in DMF, then washed with DMF, MeOH, MTBE and dried. The aminomethyl oxadiazoles of Example 18 were used without further precautions. The resins were suspended in DMF and distributed into a 96 well microtiter plate. The resin was then washed and neutralized with 5% DIEA in 1,2-dichloroethane(DCE) /THF (2:1) and washed with DCE/THF (2:1) to remove excess base. The following Isocyanates were dissolved to a concentration of 0.2 M in DCE/THF (2:1) and added to the plates. The solutions were shaken at RT overnight and then the plates were washed with DCE/THF (2:1), DMF, MeOH and dried to give N-substituted ureido oxadiazole resins.

List of Isocyanates

(2S,3S)-2-isocyanato-3-methylvaleric acid methyl ester
(R)-(+)-alpha-methylbenzyl isocyanate
(R)-(-)-1-(1-naphthyl)ethyl isocyanate

(S)-(+)-1-(1-naphthyl)ethyl isocyanate
(S)-(+)-2-isocyanato-3-tert-butoxypropionic acid methyl ester
(S)-(-)-2-isocyanato-3-methylbutyric acid methyl ester
(S)-(-)-2-isocyanato-4-(methylthio)butyric acid methyl ester
(S)-(-)-2-isocyanato-4-methylvaleric acid methyl ester
(S)-(-)-2-isocyanatoglutaric acid diethyl ester
(S)-(-)-2-isocyanatopropionic acid methyl ester
(S)-(-)-alpha-methylbenzyl isocyanate
(S)-2-isocyanato-3-phenylpropionic acid methyl ester
(Tridecafluoro-1-hexyl)isocyanate
1,1,3,3-tetramethylbutyl isocyanate
1-(1-naphthyl)ethyl isocyanate
1-(4-bromophenyl)ethyl isocyanate
1-adamantyl isocyanate
1-naphthyl isocyanate
2,3,4-trifluorophenyl isocyanate
2,3-dichlorophenyl isocyanate
2,3-dimethylphenyl isocyanate
2,4,5-trichlorophenyl isocyanate
2,4,5-trimethylphenylisocyanate
2,4,6-trichlorophenyl isocyanate
2,4-dichlorophenyl isocyanate
2,4-difluorophenyl isocyanate
2,4-dimethoxyphenyl isocyanate
2,4-dimethylphenyl isocyanate
2,5-dichlorophenyl isocyanate
2,5-difluorophenyl isocyanate
2,5-dimethoxyphenyl isocyanate
2,5-dimethylphenyl isocyanate
2,6-dibromo-4-fluorophenyl isocyanate
2,6-dibromo-4-isopropylphenyl isocyanate
2,6-dichlorophenyl isocyanate
2,6-diethylphenyl isocyanate
2,6-difluorobenzoyl isocyanate
2,6-difluorophenyl isocyanate

2,6-diisopropylphenyl isocyanate
2,6-dimethylphenyl isocyanate
2-(chloromethyl)phenyl isocyanate
2-(difluoromethoxy)phenyl isocyanate
2-(methylthio)phenyl isocyanate
2-(trifluoromethoxy)phenyl isocyanate
2-(trifluoromethyl)phenyl isocyanate
2-biphenylyl isocyanate
2-bromo-4,6-difluorophenyl isocyanate
2-bromoethyl isocyanate
2-bromophenyl isocyanate
2-chloro-4-nitrophenyl isocyanate
2-chloro-5-(trifluoromethyl)phenyl isocyanate
2-chloro-5-nitrophenyl isocyanate
2-chloro-6-methylphenyl isocyanate
2-chlorobenzyl isocyanate
2-chloroethyl isocyanate
2-chlorophenyl isocyanate
2-cyanophenyl isocyanate
2-ethoxyphenyl isocyanate
2-ethyl-6-methylphenyl isocyanate
2-ethylphenyl isocyanate
2-fluoro-3-(trifluoromethyl)phenyl isocyanate
2-fluoro-5-(trifluoromethyl)phenyl isocyanate
2-fluoro-5-methylphenyl isocyanate
2-fluoro-5-nitrophenyl isocyanate
2-fluoro-6-(trifluoromethyl)phenyl isocyanate
2-fluorophenyl isocyanate
2-iodophenyl isocyanate
2-isopropyl-6-methylphenyl isocyanate
2-isopropylphenyl isocyanate
2-methoxy-5-chloro phenyl isocyanate
2-methoxy-5-methylphenyl isocyanate
2-methoxy-5-nitrophenyl isocyanate
2-methoxyphenyl isocyanate
2-methyl-3-nitrophenyl isocyanate
2-methyl-5-nitrophenyl isocyanate

2-methyl-6-t-butylphenyl isocyanate
2-methylbenzyl isocyanate
2-n-propylphenyl isocyanate
2-naphthyl isocyanate
2-nitrophenyl isocyanate
2-phenoxyphenyl isocyanate
2-tert-butylphenyl isocyanate
3,3'-dimethoxy-4,4'-biphenylene diisocyanate
3,4,5-trimethoxyphenyl isocyanate
3,4-dichlorobenzyl isocyanate
3,4-dichlorophenyl isocyanate
3,4-difluorophenyl isocyanate
3,4-dimethylphenyl isocyanate
3,5-bis(trifluoromethyl)phenyl isocyanate
3,5-dichlorophenyl isocyanate
3,5-dimethoxyphenyl isocyanate
3,5-dimethylphenyl isocyanate
3,5-dinitrophenyl isocyanate
3-(methylthio)phenyl isocyanate
3-(trifluoromethyl)phenyl isocyanate
3-(trifluoromethylthio)phenyl isocyanate
3-acetylphenyl isocyanate
3-bromophenyl isocyanate
3-bromopropyl isocyanate
3-bromopropyl isocyanate
3-carbomethoxyphenyl isocyanate
3-chloro-2-methoxyphenyl isocyanate
3-chloro-2-methylphenyl isocyanate
3-chloro-4-fluorophenyl isocyanate
3-chloro-4-methylphenyl isocyanate
3-chlorophenyl isocyanate
3-chloropropyl isocyanate
3-cyanophenyl isocyanate
3-cyclopentoxy-4-methoxyphenyl isocyanate
3-ethylphenyl isocyanate
3-fluoro-4-methylphenyl isocyanate
3-fluorophenyl isocyanate

3-iodopropyl isocyanate
3-isocyanatobenzoyl chloride
3-isopropenyl-alpha,alpha-dimethylbenzyl isocyanate
3-methoxyphenyl isocyanate
3-methylbenzyl isocyanate
3-nitrophenyl isocyanate
3-pyridyl isocyanate
4'-isocyanato-5'-nitrobenzo-15-crown-5
4'-isocyanatobenzo-15-crown-5
4'-isocyanatobenzo-18-crown-6
4,5-dimethyl-2-nitrophenyl isocyanate
4-(6-methyl-2-benzothiazolyl)phenyl isocyanate
4-(chloromethyl)phenyl isocyanate
4-(chlorosulfonyl)phenyl isocyanate
4-(difluoromethoxy)phenyl isocyanate
4-(methylthio)phenyl isocyanate
4-(tert-butyl)phenylisocyanate
4-(trifluoromethoxy)phenyl isocyanate
4-(trifluoromethyl)phenyl isocyanate
4-(trifluoromethylthio)phenyl isocyanate
4-acetylphenyl isocyanate
4-benzyloxyphenyl isocyanate
4-bromo-2,6-dimethylphenyl isocyanate
4-bromo-2-(trifluoromethyl)phenyl isocyanate
4-bromo-2-chlorophenyl isocyanate
4-bromo-2-fluorophenyl isocyanate
4-bromo-2-methylphenyl isocyanate
4-bromophenyl isocyanate
4-chloro-2-(trifluoromethyl)phenyl isocyanate
4-chloro-2-methoxyphenyl isocyanate
4-chloro-2-methylphenyl isocyanate
4-chloro-2-nitrophenyl isocyanate
4-chloro-3-(trifluoromethyl)phenyl isocyanate
4-chloro-3-nitrophenyl isocyanate
4-chlorophenyl isocyanate
4-dimethylaminophenyl isocyanate
4-ethoxyphenyl isocyanate

4-ethylphenyl isocyanate
4-fluoro-2-(trifluoromethyl)phenyl isocyanate
4-fluoro-2-nitrophenyl isocyanate
4-fluoro-3-(trifluoromethyl)phenyl isocyanate
4-fluoro-3-nitrophenyl isocyanate
4-fluorobenzoyl isocyanate
4-fluorobenzyl isocyanate
4-fluorophenyl isocyanate
4-heptyloxyphenyl isocyanate
4-iodophenyl isocyanate
4-isocyanatobenzoyl chloride
4-isopropylphenyl isocyanate
4-methoxy-2-methylphenyl isocyanate
4-methoxybenzyl isocyanate
4-methoxyphenyl isocyanate
4-methyl-2-nitrophenyl isocyanate
4-methyl-3-nitrophenyl isocyanate
4-methylbenzyl isocyanate
4-N-butoxycarbonylphenyl isocyanate
4-N-butoxyphenyl isocyanate
4-N-butyl-2-methylphenyl isocyanate
4-N-butylphenyl isocyanate
4-nitrophenyl isocyanate
4-phenoxyphenyl isocyanate
5-bromopentyl isocyanate
5-chloro-2,4-dimethoxyphenyl isocyanate
5-chloro-2,4-toluene diisocyanate
5-chloro-o-tolyl isocyanate
5-fluoro-2-methylphenyl isocyanate
5-iodopentyl isocyanate
6,7-methylenedioxy-4-isocyanate-methylcoumarin
allyl isocyanate
benzoyl isocyanate
benzyl isocyanate
chloroacetyl isocyanate
cyclohexyl isocyanate
Ethoxycarbonyl isocyanate

Ethyl 2-isocyanato-3-methylbutyrate
Ethyl 2-isocyanato-3-phenylpropionate
Ethyl 2-isocyanato-4-(methylthio)butyrate
Ethyl 2-isocyanato-4-methylvalerate
Ethyl 2-isocyanatobenzoate
Ethyl 2-isocyanatopropionate
Ethyl 3-isocyanatobenzoate
Ethyl 3-isocyanatopropionate
Ethyl 4-isocyanatobenzoate
Ethyl 6-isocyanatohexanoate
Ethyl isocyanate
Ethyl isocyanatoacetate
Heptyl isocyanate
Hexyl isocyanate
Isobutylisocyanate
Isocyanatoethyl methacrylate
Isocyanic acid chloromethyl ester
Isopropyl isocyanate
m-tolyl isocyanate
m-xylylene diisocyanate
Mesityl isocyanate
Methyl 2-isocyanatobenzoate
Methyl isocyanate
Methylisocyanatopropionate
N-(chlorocarbonyl) isocyanate
N-butyl isocyanate
N-butyl isocyanatoacetate
N-propyl isocyanate
O-tolyl isocyanate
p-tolyl isocyanate
Pentyl isocyanate
Phenethyl isocyanate
Phenyl isocyanate
Tert-butyl 3-isothiocyanatopropionate
Tert-butyl isocyanate
Tetrahydro-2-pyranyl isocyanate
Trans-2-phenylcyclopropyl isocyanate

Trichloroacetyl isocyanate
Trichloromethyl isocyanate

EXAMPLE 22
Synthesis of Oxadiazole Thioureas

The Boc-protected Oxadiazole resins of Example 15 were treated with two portions of 50% TFA/DCM (5 min. then 30 min.), washed 3 times each with DCM, MeOH, MTBE and dried. The FMOC-protected Oxadiazole resins of Example 16 were treated with two portions of 20% piperidine in DMF, then washed with DMF, MeOH, MTBE and dried. The aminomethyl oxadiazoles of Example 18 were used without further precautions. The resins were suspended in DMF and distributed into a 96 well microtiter plate. The resin was then washed and neutralized with 5% DIEA in 1,2-dichloroethane(DCE) /THF (2:1) and washed with DCE/THF (2:1) to remove excess base. The following Isothiocyanates were dissolved to a concentration of 0.2 M in DCE/THF (2:1) and added to the plates. The solutions were shaken at RT overnight and then the plates were washed with DCE/THF (2:1), DMF, MeOH and dried to give N-substituted thioureido oxadiazole resins.

List of Isothiocyanates

(2-methoxy-5-phenyl)phenyl isothiocyanate
1-adamantyl isothiocyanate
1-naphthalenemethyl isothiocyanate
1-naphthyl isothiocyanate
2,2-diphenylethyl isothiocyanate
2,3,4,5-tetrachlorophenyl isothiocyanate
2,3,4-trichlorophenyl isothiocyanate
2,3,4-trimethoxybenzyl isothiocyanate
2,3,5,6-tetrachlorophenyl isothiocyanate
2,3,5,6-tetrafluorophenyl isothiocyanate

2,3-dibromopropyl isothiocyanate
2,3-dichlorophenyl isothiocyanate
2,3-dimethoxybenzyl isothiocyanate
2,3-dimethylphenyl isothiocyanate
2,4,5-trichlorophenyl isothiocyanate
2,4,6-tribromophenyl isothiocyanate
2,4,6-trichlorophenyl isothiocyanate
2,4,6-trifluorophenyl isothiocyanate
2,4,6-trimethylphenyl isothiocyanate
2,4-dichlorophenyl isothiocyanate
2,4-difluorophenyl isothiocyanate
2,4-dimethoxyphenyl isothiocyanate
2,4-dimethylphenyl isothiocyanate
2,5-dibromophenyl isothiocyanate
2,5-dichlorophenyl isothiocyanate
2,5-difluorophenyl isothiocyanate
2,5-dimethoxyphenyl isothiocyanate
2,5-dimethylphenyl isothiocyanate
2,6-dichlorophenyl isothiocyanate
2,6-diethylphenyl isothiocyanate
2,6-difluorophenyl isothiocyanate
2,6-diisopropylphenyl isothiocyanate
2,6-dimethylphenyl isothiocyanate
2-(3,4-dimethoxyphenyl)ethyl isothiocyanate
2-(4-chlorophenyl)ethyl isothiocyanate
2-(methylthio)phenyl isothiocyanate
2-(trifluoromethoxy)phenyl isothiocyanate
2-(trifluoromethyl)phenyl isothiocyanate
2-bromo-4-methylphenyl isothiocyanate
2-bromoethyl isothiocyanate
2-bromophenyl isothiocyanate
2-chloro-4-methylphenyl isothiocyanate
2-chloro-4-nitrophenyl isothiocyanate
2-chloro-5-(trifluoromethyl)phenyl isothiocyanate
2-chloro-5-nitrophenyl isothiocyanate
2-chloro-6-methylphenyl isothiocyanate
2-chlorobenzyl isothiocyanate

2-chloroethyl isothiocyanate
2-chlorophenyl isothiocyanate
2-cyanophenyl isothiocyanate
2-ethoxycarbonylphenyl isothiocyanate
2-ethoxyphenyl isothiocyanate
2-ethyl-6-(1-methylpropyl)phenyl isothiocyanate
2-ethyl-6-isopropylphenyl isothiocyanate
2-ethyl-6-methylphenyl isothiocyanate
2-ethylphenyl isothiocyanate
2-fluorobenzyl isothiocyanate
2-fluoroethyl isothiocyanate
2-fluorophenyl isothiocyanate
2-furfuryl isothiocyanate
2-hexyl isothiocyanate
2-iodophenyl isothiocyanate
2-isopropyl-6-methylphenyl isothiocyanate
2-isopropylphenyl isothiocyanate
2-methoxy-4-nitrophenyl isothiocyanate
2-methoxy-5-methylphenyl isothiocyanate
2-methoxy-5-nitrophenyl isothiocyanate
2-methoxybenzyl isothiocyanate
2-methoxyethyl isothiocyanate
2-methoxyphenyl isothiocyanate
2-methyl-4-nitrophenyl isothiocyanate
2-methyl-5-nitrophenyl isothiocyanate
2-methylbenzyl isothiocyanate
2-methylbutyl isothiocyanate
2-morpholinoethyl isothiocyanate
2-naphthyl isothiocyanate
2-pentyl isothiocyanate
2-phenylethyl isothiocyanate
2-piperidinoethyl isothiocyanate
2-tetrahydrofurfuryl isothiocyanate
3,4,5-trimethoxyphenyl isothiocyanate
3,4-(ethylenedioxy)phenyl isothiocyanate
3,4-dichlorobenzyl isothiocyanate
3,4-dichlorophenyl isothiocyanate

3,4-dimethoxybenzyl isothiocyanate
3,4-dimethoxyphenyl isothiocyanate
3,4-dimethylphenyl isothiocyanate
3,4-methylenedioxybenzyl isothiocyanate
3,4-methylenedioxyphenyl isothiocyanate
3,5-bis(trifluoromethyl)phenyl isothiocyanate
3,5-dichlorophenyl isothiocyanate
3,5-dimethoxyphenyl isothiocyanate
3,5-dimethylphenyl isothiocyanate
3-(diethylamino)propyl isothiocyanate
3-(methylthio)phenyl isothiocyanate
3-(trifluoromethyl)phenyl isothiocyanate
3-acetylphenyl isothiocyanate
3-benzyloxyphenyl isothiocyanate
3-bromophenyl isothiocyanate
3-bromopropyl isothiocyanate
3-carboxyphenyl isothiocyanate
3-chloro-2-methylphenyl isothiocyanate
3-chloro-4-fluorophenyl isothiocyanate
3-chloro-4-methylbenzyl isothiocyanate
3-chloro-4-methylphenyl isothiocyanate
3-chlorobenzyl isothiocyanate
3-chlorophenyl isothiocyanate
3-chloropropyl isothiocyanate
3-cyanophenyl isothiocyanate
3-dimethylaminopropylisothiocyanate
3-ethoxycarbonylphenyl isothiocyanate
3-ethylphenyl isothiocyanate
3-fluorobenzyl isothiocyanate
3-fluorophenyl isothiocyanate
3-iodophenyl isothiocyanate
3-methoxybenzyl isothiocyanate
3-methoxycarbonylphenyl isothiocyanate
3-methoxyphenyl isothiocyanate
3-methoxypropyl isothiocyanate
3-methyl-2-butyl isothiocyanate
3-methylbenzyl isothiocyanate

3-methylbutyl isothiocyanate
3-morpholinopropyl isothiocyanate
3-nitrophenyl isothiocyanate
3-pentyl isothiocyanate
3-phenylpropyl isothiocyanate
3-picolyl isothiocyanate hydrobromide
4-(benzyloxy)phenyl isothiocyanate
4-(dimethylamino)phenyl isothiocyanate
4-(methylthio)phenyl isothiocyanate
4-(trifluoromethoxy)phenyl isothiocyanate
4-(trifluoromethyl)phenyl isothiocyanate
4-acetylphenyl isothiocyanate
4-bromo-2,6-dimethylphenyl isothiocyanate
4-bromo-2-chlorophenyl isothiocyanate
4-bromo-2-methylphenyl isothiocyanate
4-bromo-2-trifluoromethylphenyl isothiocyanate
4-bromophenyl isothiocyanate
4-carboxyphenyl isothiocyanate
4-chloro-2-(trifluoromethyl)phenyl isothiocyanate
4-chloro-2-methylphenyl isothiocyanate
4-chloro-3-nitrophenyl isothiocyanate
4-chloro-3-trifluoromethylphenyl isothiocyanate
4-chlorobenzyl isothiocyanate
4-chlorophenyl isothiocyanate
4-cyanophenyl isothiocyanate
4-diethylaminophenyl isothiocyanate
4-ethoxycarbonylphenyl isothiocyanate
4-ethoxyphenyl isothiocyanate
4-ethylphenyl isothiocyanate
4-fluoro-2-methylphenyl isothiocyanate
4-fluoro-alpha-methylbenzyl isothiocyanate
4-fluorobenzyl isothiocyanate
4-fluorophenyl isothiocyanate
4-iodophenyl isothiocyanate
4-isopropylphenyl isothiocyanate
4-isothiocyanato-4'-nitrodiphenyl sulfide
4-methoxy-2-methylphenyl isothiocyanate

4-methoxy-2-nitrophenyl isothiocyanate
4-methoxybenzyl isothiocyanate
4-methoxycarbonylphenyl isothiocyanate
4-methoxyphenyl isothiocyanate
4-methyl-2-nitrophenyl isothiocyanate
4-methylbenzyl isothiocyanate
4-N-butyl-2-methylphenyl isothiocyanate
4-N-butylphenyl isothiocyanate
4-nitrophenyl isothiocyanate
4-phenoxyphenyl isothiocyanate
4-phenylazophenyl isothiocyanate
4-phenylbutyl isothiocyanate
4-sulfamoylphenyl isothiocyanate
4-tert-butylphenyl isothiocyanate
5-chloro-2,4-dimethoxyphenyl isothiocyanate
5-chloro-2-methoxyphenyl isothiocyanate
5-chloro-2-methylphenyl isothiocyanate
5-fluoro-2-methylphenyl isothiocyanate
5-indanyl isothiocyanate
5-norbornene-2-isothiocyanate
6-methyl-2-heptyl isothiocyanate
9-isothiocyanatoacridine
Allyl isothiocyanate
Allyl isothiocyanate
Alpha-methylbenzyl isothiocyanate
Alpha-methylbenzyl isothiocyanate
Benzyl isothiocyanate
Crotonyl isothiocyanate
Cycloheptyl isothiocyanate
Cyclohexanemethyl isothiocyanate
Cyclohexyl isothiocyanate
Cyclooctyl isothiocyanate
Cyclopentyl isothiocyanate
Cyclopropyl isothiocyanate
D-alpha-methylbenzyl isothiocyanate
Diethyl l-2-isothiocyanatoglutarate
Dimethyl l-isothiocyanatosuccinate

Ethyl 2-isothiocyanatopropionate
Ethyl 3-isothiocyanatobutyrate
Ethyl 3-isothiocyanatopropionate
Ethyl 4-isothiocyanatobutyrate
Ethyl isothiocyanate
Ethyl isothiocyanatoacetate
Isobutyl isothiocyanate
Isopropyl isothiocyanate
Isothiocyanatoacetaldehyde dimethyl acetal
Isothiocyanatophenyl sulfone
m-tolyl isothiocyanate
Methallyl isothiocyanate
Methoxymethyl isothiocyanate
Methyl 2-isothiocyanatoacetate
Methyl 2-isothiocyanatobenzoate
Methyl 3-isothiocyanatopropionate
Methyl dl-2-isothiocyanatobutyrate
Methyl isothiocyanate
Methyl l-2-isothiocyanato-3-methyl-butyrate
Methyl l-2-isothiocyanato-3-phenyl-propionate
Methyl l-2-isothiocyanato-4-(methylthio)butyrate
Methyl l-2-isothiocyanato-4-methyl-valerate
N-amyl isothiocyanate
N-butyl isothiocyanate
N-hexyl isothiocyanate
N-propyl isothiocyanate
Nitroscanate
Norbornyl-2-isothiocyanate
O-tolyl isothiocyanate
p-tolyl isothiocyanate
p-vinylphenyl isothiocyanate
Pentafluorophenyl isothiocyanate
Phenyl isothiocyanate
Propargyl isothiocyanate
Sec-butyl isothiocyanate
Tert-amyl isothiocyanate
Tert-butyl isothiocyanate

Tert-octyl isothiocyanate

EXAMPLE 23

Oxadiazoles derived from 2-Cyanoethylglycine (Part 1)

Boc 2-cyanoethyl glycine was loaded onto MBHA resin and converted to the Amidoxime as described in the general procedures of Example 13. This amidoxime resin was treated with a BOC amino acid anhydride as described in Example 15. The bis BOC protected oxadiazole derivative was then treated with 50 % TFA in DCM (2 X 15 min) and washed with DCM and MeOH. The diamines were then treated with 0.2 M benzoic acid, DIC, HOBT and DIEA in DCM or with acetic anhydride in DCM at RT overnight. The resin was washed with DMF 4X, DCM 2X and MeOH and dried to give the di-acylated oxadiazole resins. Alternatively, the amidoxime is treated with an FMOC amino acid anhydride as in the procedure of Example 16 to give mono-acylated-(FMOC amino)oxadiazole resins.

EXAMPLE 24

Aminomethyl Oxadiazoles derived from 2-Cyanoethylglycine (Part 2)

Boc 2-cyanoethyl glycine is loaded onto MBHA resin and converted to the oxadiazole as described in Example 17. Individual tea bags containing portions of the resulting 5-chloromethyl oxadiazole derivative are then treated with diverse amines in DMF as in Example 18. The 5-aminomethyl oxadiazole derivatives are then acylated to give the N-acylated-5-(substituted aminomethyl)oxadiazole resins, sulfonylated to give N-sulfonyl-5-(substituted aminomethyl)oxadiazole resins, alkylated to give N- alkylated-5-(substituted aminomethyl)oxadiazole resins, treated with isocyanates to give N-substituted ureidooxadiazole resins or

isothiocyanates to give N- substituted thioureidooxadiazole resins as described in Example 19, Example 20, Example 21, and Example 22. The products are then treated with 50% TFA in DCM to remove the remaining BOC group. The amino group from the groups defined above are further converted to either an amide, sulfonamide, urea or thiourea derivative following the general procedures of Example 19, Example 20, Example 21, and Example 22 to give a diverse library of oxadiazole resins.

EXAMPLE 25

Cleavage and Extraction of Products Synthesized on MBHA resin

To the dry microtiter plates containing the oxadiazole resin products was added 25 ul anisole in each well. The plates were then exposed to HF gas in an HF apparatus at RT for 1 hr. Some HF condensed in each well thus nitrogen was blown through the apparatus to remove the excess HF. The plates were then transferred to a polypropylene vacuum dessicator and evacuated overnight. The plates were then extracted into tared plates with either 1:1 Acetonitrile/water, Acetic acid or DMF. The plates containing product were lyophilized and the average yield measured. The products were analyzed by mass spectrometry and HPLC/MS.

EXAMPLE 26

Cleavage and Extraction of Products Synthesized on Wang or DAB resin

To the dry microtiter plates containing the oxadiazole resin products was added 1 ml of a solution of TFA/DCM (25 TO 50% TFA) in each well. The plates were then transferred to a vacuum centrifuge and evacuated overnight. The plates were then extracted into tared plates with either 1:1 Acetonitrile/water, Acetic acid or DMF. The plates containing product were lyophilized and the yield measured. The products were analyzed by mass spectrometry and HPLC/MS.

EXAMPLE 27

Analysis of the products

The products were analyzed by HPLC-MS using a Hewlett-Packard HPLC system hooked up to Finnigan-Mat LCQ spectrometer. FIA-MS was performed on a Sciex instrument, and HPLC was performed on a Waters HPLC system equipped with a UV detector and an evaporative light scattering detector (ELSD).

EXAMPLE 28

Preparation of carboxylic acids on solid support. (Part 1)

A resin bound amine of Example 4 and Example 5 (1.0g, 1 mmol) was treated with succinic anhydride (5 mmol) in 10 ml DCM at RT overnight. The resin teabag was washed with DCM and MTBE and dried to give the resin bound succinylated amine.

EXAMPLE 29

Preparation of carboxylic acids on solid support. (Part 2)

Wang resin (10 g, 12 mmol) was swollen in DCM for 15 min and the excess solvent poured off. A solution of carbonyl diimidazole (10 g, 50 mmol) in DCM was added and shaken for 3 hours. The solvent was poured off and the resin washed with DCM (2X) then a solution of an amino acid ester (50 mmol) and DIEA (50 mmol) in DCM was added, and the solution shaken overnight. The supernatant was removed, and the resin washed with DCM, IPA, DMF, IPA and MeOH. The resulting amino acid ester, linked to the resin through a carbamate linkage, was then treated with a solution of tetramethylammonium hydroxide (50 mmol) in DCM at RT overnight. The supernatant was removed, and the resin washed with DCM, IPA, DMF, IPA and MeOH to give the resin-bound carboxylic acid.

EXAMPLE 30

Synthesis of Amidoximes from nitriles in solution

To a solution of benzonitrile (10 mmol) in 100 ml absolute ethanol was added hydroxylamine hydrochloride (12 mmol) and K_2CO_3 (12 mmol). The solution was heated to reflux and monitored by thin layer chromatography for the disappearance of nitrile. The solution was then cooled and filtered and the solvent evaporated to give the crude benzamidoxime which was used in the next step directly. Other aliphatic, benzylic and aromatic nitriles were treated similarly to give the corresponding amidoximes.

EXAMPLE 31

Preparation of oxadiazoles from resin bound carboxylic acids

The resin bound carboxylic acids of Example 28 and Example 29, (1 g, 10 mmol) were placed in DCM and treated with 10 equivalents each of pentafluorophenol, DIEA and diisopropyl carbodiimide. After shaking for 3 hours, the solvent was poured off and the pentafluorophenyl esters were washed with 2-methoxyethyl ether and treated with a solution of 10 equivalents amidoxime from Example 30 in 2-methoxyethyl ether. The solution was heated to 60° C overnight. The solvent was then removed and the resin washed twice with 2-methoxyethyl ether and then heated to 85 %C in fresh with 2-methoxyethyl ether. The solvent was removed and the resin washed with MeOH and dried to give oxadiazole resins.

EXAMPLE 32

Preparation of Oxadiazole combinatorial libraries: Synthesis of TRG 3600

Five carboxylic acid nitriles were coupled to 15 g of MBHA resin each as described in Example 3. Each nitrile resin was then distributed to 36 teabags and sets of 5 teabags were converted to oxadiazole derivatives by conversion to the amidoxime as in Example 13, and each amidoxime was reacted with 36 different Boc amino acids to give 180 different oxadiazole intermediates as described in Example 15. Each of the 180 intermediates was deprotected by treatment with 50% TFA/DCM, and each resin was transferred to a 96 well reaction block. Each intermediate in the reaction block was then treated with 96 carboxylic acids from Example 19. The final products were then cleaved from the resin with HF, extracted from the resin using acetic acid and lyophilized as described

in Example 25. An aliquot of each product was taken and analyzed by mass spectrometry and HPLC with UV and ELSD detection. This created 17280 oxadiazole amide products which correspond to all permutations of the reagents listed below.

Carboxylic acid nitriles:

Cyanoacetic acid
1-Cyano-1-cyclopropane carboxylic acid
3-Cyanobenzoic acid
4-Cyanobenzoic acid
2-(4-Cyanophenoxy)-2-methyl propionic acid

Boc amino acids:
Boc-Alanine-OH
Boc-b-Alanine-OH
Boc-3-(Pyridyl)-Alanine-OH
Boc-2-(Thienyl)-Alanine-OH
Boc-a-Aminobutyric Acid-OH
Boc-g-Aminobutyric Acid-OH
Boc-e-Aminocaproic Acid-OH
Boc-a-Aminoisobutyric Acid-OH
Boc-trans-4-(Aminomethyl)-Cylohexane Carboxylic Acid-OH
Boc-Arginine(Tos)-OH
Boc-Aspartic Acid-OBzl
Boc-Aspartic Acid(OcHex)-OH
Boc-3-Carboxymethyl-1-Phenyl-1,3,8-triazaspiro[4.5]decane-4-one-OH
Boc-4-Chlorophenylalanine-OH
Boc-Cyclohexylalanine-OH
Boc-Glutamic Acid-OBzl
Boc-Glutamic Acid(OcHex)-OH
Boc-Glycine-OH
Boc-Histidine(Tos)-OH
Boc-Isoleucine-OH Hemihydrate
Boc-Isonipecotic Acid-OH

Boc-Leucine-OH Hydrate
Boc-Nipecotic Acid-OH
Boc-Norleucine-OH
Boc-Phenylalanine-OH
Boc-D,L-Pipecolinic Acid-OH
Boc-Proline-OH
Boc-Serine(Bzl)-OH
Boc-Thioproline-OH
Boc-Threonine(Bzl)-OH
Boc-TIC-OH
Boc-Tryptophan(For)-OH
Boc-Tyrosine(Bzl)-OH
Boc-OEt-Tyrosine-OH
Boc-Valine-OH
N-Fmoc-Lysine(Boc)-OH

Carboxylic acids:

Acetic acid
alpha-Methylcinnamic acid
Benzoic acid
Crotonic acid
Cyclobutanecarboxylic acid
Cyclohexanepropionic acid
4-Cyanobenzoic acid
Hydrocinnamic acid
4-Dimethylaminobenzoic acid
4-Ethoxybenzoic acid
Isobutyric acid
4-Ethoxyphenylacetic acid
Isovaleric acid
Levulinic acid
m-Anisic acid
m-Toluic acid
Methoxyacetic acid
Isonicotinic acid
p-Tolylacetic acid

Picolinic acid
Piperonylic acid
4-Fluoro-alpha-methylphenylacetic acid
4-Fluorophenylacetic acid
Tetrahydro-3-furoic acid
trans-3-(3-Pyridyl)acrylic acid
Trimethylacetic acid
Triphenylacetic acid
Nicotinic acid
(3,4-Dimethoxyphenyl)Acetic acid
Boc-isonipecotic acid
(alpha-alpha-alpha-Trifluoro-m-Tolyl)acetic acid
(Methylthio)acetic acid
(Phenylthio)acetic acid
1-(4-Chlorophenyl)-1-Cyclopentanecarboxylic acid
1-Adamantaneacetic acid
1-Naphthylacetic acid
1-Phenyl-1-Cyclopropanecarboxylic acid
4-Iodobenzoic acid
4-Isopropoxybenzoic acid
2,4-Dichlorobenzoic acid
4-Methyl-1-Cyclohexanecarboxylic acid
Pyrrole-2-carboxylic acid
4-Methylvaleric acid
1-Naphthylacetic acid
2-Fluorobenzoic acid
1,3-phenylene diacetic acid
2-Norbornaneacetic acid
2-Pyrazinecarboxylic acid
2-Pyridylacetic acid hydrochloride
2-Thiopheneacetic acid
3,4,5-Triethoxybenzoic acid
3,4-(Methylenedioxy)-Phenylacetic acid
3,4-Dichlorobenzoic acid
4-Isopropylbenzoic acid
3,4-Dichlorophenylacetic acid
4-tert-Butyl-cyclohexanecarboxylic acid

4-carboxybenzenesulfonamide
3,5,5-Trimethylhexanoic acid
3,5-Bis(Trifluoromethyl)-Benzoic acid
5-Bromo-2-chlorobenzoic acid
5-Bromonicotinic acid
6-Chloronicotinic acid
3,5-Dimethyl-p-anisic acid
3-Bromo-4-Methylbenzoic acid
3,4,5-Trimethoxyphenylacetic acid
3-Benzoylpropionic acid
3,5-Dichlorobenzoic acid
3-Cyanobenzoic acid
3-Fluoro-4-Methylbenzoic acid
1-Isoquinolinecarboxylic acid
3-Methyl-2-thiophenecarboxaldehyde
3-Phenoxybenzoic acid
3-Thiopheneacetic acid
4-Biphenylacetic acid
4-Bromophenylacetic acid
S-(+)-Mandelic acid
3,5-Di-tert-butyl-4-hydroxybenzoic acid
3,5-Dichloro-4-hydroxybenzoic acid
4-Hydroxybenzoic acid
5-Methylsalicylic acid
2-Methylcyclopropanecarboxylic acid
3-Indolepropionic acid
diphenylacetic acid
5-Methoxyindole-2-carboxylic acid
succinamic acid
4-(dimethylamino)butyric acid hydrochloride
4-(methylthio)benzoic acid
2-(methylthio)nicotinic acid
R(-)-2-oxothiazolidine-4-carboxylic acid
4-nitrophenylacetic acid
coumarin-3-carboxylic acid
1-cyano-1-cyclopropane carboxylic acid
2-chloro-5-(methylthio)benzoic acid

theophylline-7-acetic acid
2-(2-cyanophenylthio)benzoic acid

EXAMPLE 33

Preparation of Oxadiazole combinatorial libraries:
Synthesis of TRG 3900

Five carboxylic acid nitriles were coupled to 15 g of MBHA resin each as described in Example 3. Each nitrile resin was then distributed to 36 teabags and sets of 5 teabags were converted to oxadiazole derivatives by conversion to the amidoxime as in Example 13, and each amidoxime was reacted with 36 different Boc amino acids to give 180 different oxadiazole intermediates as described in Example 15. Each of the 180 intermediates was deprotected by treatment with 50% TFA/DCM, and each resin was transferred to one half of a 96 well reaction block. Each of the 180 intermediates was then reacted with 48 sulfonyl chlorides following Example 20. The final products were then cleaved from the resin with HF, extracted from the resin using acetic acid and lyophilized as described in Example 25. An aliquot of each product was taken and analyzed by mass spectrometry and HPLC with UV and ELSD detection. This created 8640 oxadiazole sulfonamide products corresponding to all permutations of the reagents listed below.

Carboxylic acid nitriles:

Cyanoacetic acid
1-Cyano-1-cyclopropane carboxylic acid
3-Cyanobenzoic acid
4-Cyanobenzoic acid
2-(4-Cyanophenoxy)-2-methyl propionic acid

Boc amino acids:

Boc-Alanine-OH
Boc-b-Alanine-OH
Boc-3-(Pyridyl)-Alanine-OH
Boc-2-(Thienyl)-Alanine-OH
Boc-a-Aminobutyric Acid-OH
Boc-g-Aminobutyric Acid-OH
Boc-e-Aminocaproic Acid-OH
Boc-a-Aminoisobutyric Acid-OH
Boc-trans-4-(Aminomethyl)-Cylohexane Carboxylic Acid-OH
Boc-Arginine(Tos)-OH
Boc-Aspartic Acid-OBzl
Boc-Aspartic Acid(OcHex)-OH
Boc-3-Carboxymethyl-1-Phenyl-1,3,8-
triazaspiro[4.5]decane-4-one-OH
Boc-4-Chlorophenylalanine-OH
Boc-Cyclohexylalanine-OH
Boc-Glutamic Acid-OBzl
Boc-Glutamic Acid(OcHex)-OH
Boc-Glycine-OH
Boc-Histidine(Tos)-OH
Boc-Isoleucine-OH Hemihydrate
Boc-Isonipecotic Acid-OH
Boc-Leucine-OH Hydrate
Boc-Nipecotic Acid-OH
Boc-Norleucine-OH
Boc-Phenylalanine-OH
Boc-D,L-Pipecolinic Acid-OH
Boc-Proline-OH
Boc-Serine(Bzl)-OH
Boc-Thioproline-OH
Boc-Threonine(Bzl)-OH
Boc-TIC-OH
Boc-Tryptophan(For)-OH
Boc-Tyrosine(Bzl)-OH
Boc-OEt-Tyrosine-OH
Boc-Valine-OH
N-Fmoc-Lysine(Boc)-OH

List of Sulfonyl chlorides:

2-mesitylenesulfonyl chloride
2-naphthalenesulfonyl chloride
2-thiophenesulfonyl chloride
4-chlorobenzenesulfonyl chloride
4-fluorobenzenesulfonyl chloride
4-methoxybenzenesulfonyl chloride
4-methylsulfonylbenzenesulfonyl chloride
Benzenesulfonyl chloride
Dansyl chloride
N-acetylsulfanilyl chloride
2-acetamido-4-methyl-5-thiazolesulfonyl chloride
4-(trifluoromethoxy)benzenesulphonyl chloride
4-tert-butylbenzenesulfonyl chloride
8-quinolinesulfonyl chloride
2,3-dichlorothiophene-5-sulphonyl chloride
3,4-dimethoxybenzenesulfonyl chloride
3,5-di(trifluoromethyl)benzenesulphonyl chloride
3-chloro-4-fluorobenzenesulphonyl chloride
3-trifluoromethylbenzenesulphonyl chloride
4-ethylbenzenesulfonyl chloride
Pentamethylbenzenesulfonyl chloride
2,3,4-trifluorobenzenesulphonyl chloride
2,4-dichlorobenzenesulfonyl chloride
2,5-dichlorothiophene-3-sulphonyl chloride
2,6-dichlorobenzenesulfonyl chloride
2,6-difluorobenzenesulphonyl chloride
2-chloro-4-(trifluoromethyl)benzenesulphonyl chloride
2-chloro-5-(trifluoromethyl)benzenesulphonyl chloride
2-chloro-6-methylbenzenesulphonyl chloride
3,4-difluorobenzenesulphonyl chloride
3,5-dichlorobenzenesulfonyl chloride
3-chlorobenzenesulfonyl chloride
4-(N-butoxy)benzenesulphonyl chloride
4-trifluoromethylbenzene sulphonyl chloride
3,5-dimethylisoxazole-4-sulfonyl chloride

2-(methoxycarbonyl)thiophene-3-sulfonyl chloride
4-acetamido-3-chlorobenzene sulfonyl chloride
2-[1-methyl-5-(trifluoromethyl)pyrazol-3-yl]thiophene-5-sulfonyl chloride
2-(benzoylaminomethyl)thiophene-5-sulfonyl chloride
3-methoxy-4-(methoxycarbonyl)-thiophene-2-sulphonyl chloride
5-(isoxazol-3-yl)thiophene-2-sulphonyl chloride
4-cyanobenzene sulfonyl chloride
3-chloro-4-methylbenzenesulfonyl chloride
2,4-difluorobenzenesulfonyl chloride
2-fluorobenzenesulphonyl chloride
4-isopropylbenzene sulphonyl chloride
2,5-dimethoxybenzenesulfonyl chloride
3,4-dichlorobenzenesulfonyl chloride

EXAMPLE 34

Preparation of Oxadiazole combinatorial libraries: Synthesis of TRG 4000

Four carboxylic acid nitriles were coupled to 100g of MBHA resin each as described in Example 3. Each nitrile resin was then distributed to 24 teabags and sets of 4 teabags were converted to oxadiazole derivatives by conversion to the amidoxime as in Example 13, and each amidoxime was reacted with 24 different Boc amino acids to give 96 different oxadiazole intermediates as described in Example 15. Each of the 96 intermediates was deprotected by treatment with 50% TFA/DCM, and each resin was transferred to a 96 well reaction block. Each intermediate in the reaction block was then treated with 80 carboxylic acids from Example 19, and 16 isocyanates from the list below as described in Example 21. The final products were then cleaved from the resin with HF, extracted from the resin using acetic acid and lyophilized as described in Example 25. An aliquot of each product was taken and analyzed by mass spectrometry and HPLC with UV and ELSD detection. This created 9216 oxadiazole amide and urea products which correspond to all permutations of the reagents listed below.

List of Carboxylic acid nitriles:

1-Cyano-1-cyclopropane carboxylic acid
3-Cyanobenzoic acid
4-Cyanobenzoic acid
2-(4-Cyanophenoxy)-2-methyl propionic acid

List of Amino Acids

Boc-Alanine-OH
Boc-3-(Pyridyl)-Alanine-OH
Boc-a-Aminobutyric Acid-OH
Boc-g-Aminobutyric Acid-OH
Boc-a-Aminoisobutyric Acid-OH
Boc-Arginine(Tos)-OH
Boc-Aspartic Acid(OcHex)-OH
Boc-3-Carboxymethyl-1-Phenyl-1,3,8-triazaspiro[4.5]decane-4-one-OH
Boc-4-Chlorophenylalanine-OH
Boc-Cyclohexylalanine-OH
Boc-Glutamic Acid-OBzl
Boc-Histidine(Tos)-OH
Boc-Isoleucine-OH
Boc-Isonipecotic Acid-OH
Boc-Leucine-OH
Boc-Nipecotic Acid-OH
Boc-Norleucine-OH
Boc-Phenylalanine-OH
Boc-D,L-Pipecolinic Acid-OH
Boc-Proline-OH
Boc-Serine(Bzl)-OH
Boc-Threonine(Bzl)-OH
Boc-OEt-Tyrosine-OH
Boc-Valine-OH

List of Carboxylic acids

Acetic acid
alpha-Methylcinnamic acid
Benzoic acid
Crotonic acid
Cyclohexanepropionic acid
4-Cyanobenzoic acid
Hydrocinnamic acid

4-Dimethylaminobenzoic acid
Isobutyric acid
Isonicotinic acid
4-Ethoxyphenylacetic acid
Isovaleric acid
Levulinic acid
m-Anisic acid
m-Toluic acid
Methoxyacetic acid
Nicotinic acid
p-Tolylacetic acid
Picolinic acid
Piperonylic acid
4-Fluorophenylacetic acid
Tetrahydro-3-furoic acid
trans-3-(3-Pyridyl)acrylic acid
Trimethylacetic acid
Triphenylacetic acid
(3,4-Dimethoxyphenyl)Acetic acid
(alpha-alpha-alpha-Trifluoro-m-Tolyl)acetic acid
(Methylthio)acetic acid
1-(4-Chlorophenyl)-1-Cyclopentanecarboxylic acid
1-Adamantaneacetic acid
1-Naphthylacetic acid
1-Phenyl-1-Cyclopropanecarboxylic acid
4-Iodobenzoic acid
4-Isopropoxybenzoic acid
4-Isopropylbenzoic acid
2,4-Dichlorobenzoic acid
4-Methyl-1-Cyclohexanecarboxylic acid
4-Methylvaleric acid
2-Fluorobenzoic acid
2-Methylcyclopropanecarboxylic acid
2-Norbornaneacetic acid
2-Pyrazinecarboxylic acid
2-Thiopheneacetic acid
3,4-Dichlorobenzoic acid

3,4-Dichlorophenylacetic acid
4-tert-Butyl-cyclohexanecarboxylic acid
3,5,5-Trimethylhexanoic acid
5-Bromo-2-chlorobenzoic acid
5-Bromonicotinic acid
6-Chloronicotinic acid
3,4,5-Trimethoxyphenylacetic acid
3-Benzoylpropionic acid
3-Bromo-4-Methylbenzoic acid
3-Cyanobenzoic acid
3-Fluoro-4-Methylbenzoic acid
3-Methyl-2-thiophenecarboxaldehyde
3-Phenoxybenzoic acid
4-Biphenylacetic acid
4-Bromophenylacetic acid
S-(+)-Mandelic acid
3,5-Di-tert-butyl-4-hydroxybenzoic acid
3,5-Dichloro-4-hydroxybenzoic acid
5-Methylsalicylic acid
3-Indolepropionic acid
5-Methoxyindole-2-carboxylic acid
1-cyano-1-cyclopropane carboxylic acid
succinamic acid
4-(dimethylamino)butyric acid hydrochloride
4-(methylthio)benzoic acid
2-(methylthio)nicotinic acid
4-nitrophenylacetic acid
coumarin-3-carboxylic acid
4-carboxybenzenesulfonamide
2-chloro-5-(methylthio)benzoic acid
theophylline-7-acetic acid
2-(2-cyanophenylthio)benzoic acid
R(-)-2-oxothiazolidine-4-carboxylic acid
diphenylacetic acid
DL-2-(3-Chlorophenoxy)-propionic acid
4-Phenoxybenzoic acid

List of isocyanates:

1-adamantyl isocyanate
1-naphthyl isocyanate
2,4-difluorophenyl isocyanate
2,4-dimethoxyphenyl isocyanate
2,4-dimethylphenyl isocyanate
2,6-diisopropylphenyl isocyanate
2-ethyl-6-isopropylphenyl isocyanate
2-methoxy-5-nitrophenyl isocyanate
2-methyl-4-nitrophenyl isocyanate
2-phenylphenyl isocyanate
3,5-dicarbomethoxyphenyl isocyanate
3,5-dichlorophenyl isocyanate
3-acetylphenyl isocyanate
3-chlorophenyl isocyanate
3-fluorophenyl isocyanate
3-trifluoromethylphenyl isocyanate
4-(trifluoromethoxy)phenyl isocyanate
4-chlorophenyl isocyanate
4-cyanophenyl isocyanate
4-fluoro-3-nitrophenyl isocyanate
4-fluorophenyl isocyanate
4-methoxyphenyl isocyanate
4-N-carbobutoxyphenyl isocyanate
4-nitrophenyl isocyanate
4-phenoxyphenyl isocyanate
5-chloro-2,4-dimethoxyphenyl isocyanate
5-chloro-2-methoxyphenyl isocyanate
Ethyl 4-isocyanato benzoate
Isopropyl isocyanate
m-tolyl isocyanate
N-(methoxycarbonyl)isocyanate
N-amyl isocyanate
Phenethyl isocyanate
Phenyl isocyanate

EXAMPLE 35

Preparation of Oxadiazole combinatorial libraries: Synthesis of TRG 5500

The cyanophenols listed below were coupled to 300 g each of Wang bromide resin to give the corresponding cyanophenyl ethers, following the procedure of Example 9. 600g of resin bound piperazine prepared in Example 5 was converted to 300 g of resin bound 4-cyanobenzyl piperazine following Example 8, and 300 g of resin bound 4-cyanophenoxyacetyl piperazine according to the procedures of Example 7 and Example 10. The seven resulting resin bound nitriles were converted to the amidoxime as described in the general procedure of Example 12. The amidoximes were converted to the 5-chloromethyl oxadiazoles as described in Example 17. Each chloromethyl oxadiazole resin was reacted with the 60 primary amines listed below following the procedure of Example 18 to give 420 aminomethyl oxadiazole intermediates. Each of the 420 intermediates was reacted with 80 carboxylic acids to give the amide derivatives and 48 sulfonyl chlorides to give sulfonamides according to the procedures of Example 19 and Example 20 respectively. The final products were cleaved from the resin with 50% TFA/DCM, and evaporated. The products were extracted from the resin using acetic acid and lyophilized as described in Example 25. An aliquot of each product was taken and analyzed by mass spectrometry and HPLC with UV and ELSD detection.

List of Cyanophenols:

1	4-hydroxy-3-methoxybenzonitrile
2	4-cyanophenol
3	2-fluoro-4-hydroxybenzonitrile
4	3-cyanophenol
5	4-cyano-4'-hydroxybiphenyl

List of amines:

1	1-(2-Aminoethyl)pyrrolidine
2	2-(Aminomethyl)pyridine
3	Histamine
4	Cyclopentylamine
5	Allylamine
6	2-Methoxyethylamine
7	(Å)-Tetrahydrofurylamine
8	Benzylamine
9	2-Methylbenzylamine
10	3-Methylbenzylamine
11	4-Methylbenzylamine
12	2-Fluorobenzylamine
13	3-Fluorobenzylamine
14	4-Fluorobenzylamine
15	1-(3-Aminopropyl)imidazole
16	p-Xylylenediamine,
17	4-Methoxybenzylamine
18	3-Chlorobenzylamine
19	3-Bromobenzylamine HCl
20	4-Bromobenzylamine HCl
21	Cyclopropylamine
22	(Aminomethyl)cyclopropane
23	4-(Aminomethyl)pyridine
24	3-(Aminomethyl)pyridine
25	2-Thiophenemethylamine
26	Phenethylamine
27	4-(2-Aminoethyl)morpholine
28	3-Methoxybenzylamine
29	Piperonylamine
30	4-Methoxyphenethylamine
31	2-Fluorophenethylamine
32	2-(4-Chlorophenyl)ethylamine
33	2-(3-Chlorophenyl)ethylamine
34	2-(2-Chlorophenyl)ethylamine
35	2,3-Dimethoxybenzylamine

36	3,4-Dimethoxyphenethylamine
37	2,4-Dichlorophenethylamine
38	N,N-Diethylethylenediamine
39	2-(2-Aminoethyl)-1-methylpyrrolidine
40	3-Diethylaminopropylamine
41	2-(2-Aminoethylamino)-5-nitropyridine
42	N,N,2,2-Tetramethyl-1,3-propanediamine
43	3-Dimethylaminopropylamine
44	Ethylenediamine
45	1-(2-Aminoethyl)piperidine
46	isoamylamine
47	3-Ethoxypropylamine
48	1-(3-Aminopropyl)-2-pipecoline
49	3-Butoxypropylamine
50	N-(3'-Aminopropyl)-2-pyrrolidinone, tech
51	4-(3-Aminopropyl)morpholine
52	N-(2-Aminoethyl)-N-ethyl-m-toluidine
53	3-Phenyl-1-propylamine
54	b-Methylphenethylamine
55	4-Phenylbutylamine
56	3,3-Diphenylpropylamine
57	Isobutylamine
58	2-(2-Aminoethyl)pyridine
59	Cyclohexanemethylamine
60	3-Methoxyphenethylamine
61	3-Phenylbenzylamine

EXAMPLE 36

Anti-microbial Screen

Streptococcus pyogenes (ATCC# 97-03 14289) were grown in Todd Hewitt Broth (THB) (Difco Laboratories #0492-17-6) overnight until they reached an optical density of (OD = 0.636@ 570 nm) by reading 0.1 ml in a 96 well microtiter plate in a Molecular Devices Thermomax. This preparation was kept frozen as stocks in 30% v/v glycerol in 1.5 ml aliquots at -70 C° until use.

Prior to screening, 1.5 ml aliquots were thawed and diluted into 50 ml THB. 200 ul of this dilution was added to 92 wells of microtiter plate. To three wells THB (200 ul) was added to serve as a blank and a sterility control. Test compounds in DMSO and appropriate concentrations of DMSO were added to Growth/Solvent Controls at 0 time. Plates were read at 0 time at 570 nm in the Molecular Devices plate reader to obtain compounds correction factors for insoluble or colored compounds. Plates were read again at 4 hrs.

Compounds listed in the table below are described in reference to Formula (I), wherein the ring structure is a 1, 2, 4 oxadiazole (where U is an oxygen), R_1 corresponds to the starting material of X_1 and X_2, R_2 corresponds to the starting material of X_3 and R_3 corresponds to the starting material of X_4. The compounds were assayed at a concentration of 170 μg/ml. Percent inhibition for each compound was calculated using the following formulae:

Color correct =
(O.D. 0 hr - Blank 0 hr)-(Solvent Control 0 hr - Blank 0 hr)

% Inhibition =
100 - (O.D. test compound 4 hr - Blank 4 hr - color correct) divided by (O.D. growth/solvent control 4 hr - Blank 4 hr)

Pool	R_1	R_2	R_3
6226	1-cyano-1-cyclopropane-cooh	boc-3-carboxymethyl-1-phenyl-1,3,8-triazaspiro[4,5]decane-4-one	alpha-methylcinnamic acid
6229	1-cyano-1-cycloprpane-cooh	boc-3-carboxymethyl-1-phenyl-1,3,8-triazaspiro[4.5]decane-4-one	cyclohexanepropionic acid
4119	1-cyano-1-cyclopropane-cooh	boc-threonine(Bzl)	hydrocinnamic acid
1769	2-(4-cynophenoxy)-2-methyl-propionic	boc-cyclohexylalanine	isobutyric acid
2762	3-cyanobenzoic acid	boc-a-aminoisobutyric acid	isonicotinic acid
2604	3-cyanobenzoic acid	boc-3-(pridyl)-alanine	isovaleric acid
1773	2-(4-cyanophenoxy)-2-methyl-propionic	boc-cyclohexylalanine	levulinic acid
2846	3-cycanobenzoic acid	boc-aspartic acid(ochex)	m-anisic acid
6239	1-cyano-1-cyclopropane-cooh	boc-3-carboxymethyl-1-phenyl-1,3,8-triazaspiro[4.5]decane-4-one	m-toluic acid

4130	1-cyano-1-cyclopropane-cooh	boc-threonine(bzl)	p-tolylacetic acid
4291	2-(4-cyanophenoxy)-2-methyl-propionic	boc-3-carboxymethyl-1-henyl-1,3,8-triazaspiro[4.5]decane-4-one	picolinic acid
3012	3-Cyanobenzoic acid	Boc-Cyclohexylalanine	Piperonylic acid
2812	3-cyanobenzoic	Boc-a-aminoisobutyric acid	S-(+)-mandelic acid
7046	2-(4-Cyanophenoxy)-2-Methyl-propionic	acid Boc-4-Chlorophenylalanine	Tetrahydro-3-furoic acid
4695	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-OEt-Tyrosine	trans-3-(3-Pyridyl)acrylic acid
3417	4-Cyanobenzoic acid	Boc-Histidine(Tos)	Triphenylacetic acid
3978	1-Cyano-1-Cyclopropane-COOH	Boc-Phenylalanine	(3,4-Dimethoxyphenyl)Acetic acid"
4379	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Histidine(Tos)	(alpha-alpha-alpha-Trifluoro-m-Tolyl)acetic acid

5

4300	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-3-Carboxymethyl-1-Phenyl-1,3,8-triazaspiro[4.5]decne-4-one	(Methylthio)acetic acid
1149	1-Cyano-1-Cyclopropane-COOH	Boc-3-(Pyridyl)-Alanine	1-(4-Chlorophenyl)-1-Cyclopentanecarboxylic acid
1230	1-Cyano-1-Cyclopropane-COOH	Boc-a-AminobutyricAcid	1-Adamantaneacetic acid
7490	4-Cyanobenzoic acid	Boc-Glutamic Acid-OBzl	1-adamantylisocyanate
4098	1-Cyano-1-Cyclopropane-COOH	Boc-Proline	1-cyano-1-cyclopropane carboxylic acid
4383	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Histidine(Tos)	1-Naphthylacetic acid
2788	3-Cyanobenzoic acid	Boc-a-Aminoisobutyric Acid	2,4-Dichlorobenzoic acid
7684	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-a-Aminobutyric Acid	2,4-difluorophenyl isocyanate
4933	4-Cyanobenzoic acid	Boc-Leucine	2,4-dimethylphenyl isocyanate
2519	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Cyclohexylalanine	2,6-diisopropylphenyl isocyanate

3148	3-Cyanobenzoic acid	Boc-Isoleucine	2-(2-cyanophenylthio)benzoic acid
4502	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Isonipecotic Acid	2-(methylthio)nicotinic acid
4266	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Alanine	2-chloro-5-(methylthio) benzoic acid
7462	4-Cyanobenzoic acid	Boc-a-Aminobutyric Acid	2-METHYL-4-NITROPHENYL ISOCYANATE
1800	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Cyclohexylalanine	2-Methylcyclopropanecarboxylic acid
7817	3-Cyanobenzoic acid	Boc-Glutamic Acid-OBzl	2-Norbornaneacetic acid
3674	1-Cyano-1-Cyclopropane-COOH	Boc-g-Aminobutyric Acid	2-Pyrazinecarboxylic acid
4475	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Isonipecotic Acid	2-Thiopheneacetic acid
2963	3-Cyanobenzoic acid	Boc-3-Carboxymethyl-1-Phenyl-1,8-triazaspiro [4.5]decane-4-one	3,4,5-Trimethoxyphenylacetic acid
1244	1-Cyano-1-Cyclopropane-COOH	Boc-a-Aminobutyric Acid	3,4-Dichlorobenzoic acid

3037	3-Cyanobenzoic acid	Boc-Cyclohexylalanine	3,4-Dichlorophenylaceti c acid
2879	3-Cyanobenzoic acid	Boc-Aspartic Acid(OcHex)	3,5,5-Trimethylhexanoic acid
2653	3-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	3,5-Di-tert-butyl-4-hyd roxybenzoic acid
5034	1-Cyano-1-Cyclopropane-C OOH	Boc-Phenylalanine	3,5-dica rbomethoxyphenyl isocyanate
5726	4-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	3,5-Dichloro-4-hydroxyb enzoic acid
7577	1-Cyano-1-Cyclopropane-C OOH	Boc-4-Chlorophenylalanine	3,5-dichlorophenyl isocyanate
7691	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-a-Aminobutyric Acid	3-(trifluoromethyl)phen yl isocyanate
3044	3-Cyanobenzoic acid	Boc-Cyclohexylalanine	3-Benzoylpropionic acid
5317	3-Cyanobenzoic acid	Boc-a-Aminobutyric acid	3-Bromo-4-Methylbenzoic acid
2162	3-Cyanobenzoic acid	Boc-4-Chlorophenylalanine	3-chlorophenyl isocyanate
2646	3-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	3-Cyanobenzoic acid
4087	1-Cyano-1-Cyclopropane-C OOH	Boc-Proline	3-Fluoro-4-Methylbenzoi c acid

7370	3-Cyanobenzoic acid	Boc-a-Aminobutyric Acid	3-fluorophenyl isocyanate
8080	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Proline	3-Indolepropionic acid
1816	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Cyclohexylalanine	3-Methyl-2-thiophenecarboxylic acid
2649	3-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	3-Phenoxybenzoic acid
2660	3-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	4-(dimethylamino)butyric acid hydrochloride
7093	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-4-Chlorophenylalanine	4-(methylthio)benzoic acid
7676	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-3-(Pyridyl)-Alanine	4-(trifluoromethoxy)phenyl isocyanate
1178	1-Cyano-1-Cyclopropane-COOH	Boc-3-(Pyridyl)-Alanine	4-Biphenylacetic acid

4491	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Isonipecotic Acid	4-Bromophenylacetic acid
5010	1-Cyano-1-Cyclopropane-COOH	Boc-Isoleucine	4-chlorophen Yl isocyanate
3478	4-Cyanobenzoic acid	Boc-Leucine	4-Cyanobenzoic acid
4796	3-Cyanobenzoic acid	Boc-a-Aminoisobutyric Acid	4-cyanophenyl isocyanate
8326	4-Cyanobenzoic acid	Boc-Valine	4-Dimethylaminobenzoic acid
2843	3-Cyanobenzoic acid	Boc-Aspartic Acid(OcHex)	4-Ethoxyphenylacetic acid
2474	1-Cyano-1-Cyclopropane-COOH	Boc-Leucine	4-fluoro-3-nitr Ophenyl isocyanate
2163	3-Cyanobenzoic acid	Boc-4-Chlorophenylalanine	4-fluorophenyl isocyanate
4613	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Nipecotic Acid	4-Fluorophenylacetic acid
2626	3-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	4-Isopropoxybenzoic acid
2787	3-Cyanobenzoic acid	Boc-a-Aminoisobutyric Acid	4-Isopropylbenzoic acid

4389	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Histidine(Tos)	4-Methyl-1-Cyclohexanecarboxylic acid
598	4-Cyanobenzoic acid	Boc-3-Carboxymethyl-1-Phenyl-1,3,8-triazaspiro[4.5]decane-4-one	4-Methylvaleric acid
4941	4-Cyanobenzoic acid	Boc-Leucine	4-n-carbobutoxyphenyl Isocyanate
2447	1-Cyano-1-Cyclopropane-COOH	Boc-Cyclohexylalanine	4-nit Rophenyl isocyanate
4103	1-Cyano-1-Cyclopropane-COOH	Boc-Proline	4-nitrophenylacetic acid
3552	4-Cyanobenzoic acid	Boc-Leucine 4-Phenoxybenzoic acid	4-Phenoxybenzoic acid
4814	3-Cyanobenzoic acid	Boc-Aspartic Acid(OcHex)	Acid(ochex)4-phenoxyphenyl isocyanate
4478	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Isonipecotic Acid	4-tert-Butyl-cyclohexanecarboxylic acid
3521	4-Cyanobenzoic acid	Boc-Leucine	5-Bromonicotinic acid
2300	4-Cyanobenzoic acid	Boc-Isonipecotic Acid	5-chloro-2,4-dimethoxyphenyl isocyanate

2397	1-Cyano-1-Cyclopropane-COOH	Boc-3-(Pyridyl)-Alanine	5-Chloro-2-methoxyphenyl isocyanate
3457	4-Cyanobenzoic acid	Boc-Histidine(Tos)	5-Methoxyindole-2-carboxylic acid
4575	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Leucine	5-Methylsalicylic acid
2882	3-Cyanobenzoic acid	Boc-Aspartic	Acid(OcHex) 6-Chloronicotinic acid
2904	3-Cyanobenzoic acid	Boc-Aspartic Acid(OcHex)	coumarin-3-carboxylic acid
1198	1-Cyano-1-Cyclopropane-COOH	Boc-3-(Pyridyl)-Alanine	diphenylacetic acid
3551	4-Cyanobenzoic acid	Boc-Leucine	DL-2-(3-Chlorophenoxy)-propionic acid
7584	1-Cyano-1-Cyclopropane-COOH	Boc-4-Chlorophenylalanine	Ethyl 4-isocyanatobenzoate
7443	4-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	ISOPROPYL ISOCYANATE
2574	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Serine(Bzl)	N-(methoxycarbonyl)isocyanate
7437	3-Cyanobenzoic acid	Boc-Leucine	Pentyl isocyanate
7454	4-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	Phenethyl

2197	3-Cyanobenzoic acid	Boc-Phenylalanine	Phenyl isocyanate
8093	2-(4-Cyanophenoxy)-2-Methyl-propionic acid	Boc-Proline	R(-)-2-oxothiazolidine-4-carboxylic acid
2659	3-Cyanobenzoic acid	Boc-3-(Pyridyl)-Alanine	succinamic acid
4187	1-Cyano-1-Cyclopropane-COOH	Boc-Threonine(Bzl)	theophyl line-7-acetic acid

EXAMPLE 37

Preparation of 1,3,4-Oxadiazoles

The resin bound carboxylic acids of examples 28 and 29 are placed in a solution of 4-nitrophenyl trifluoroacetate (10 equivalents) in DCM and shaken at RT for 6 hours to give the corresponding 4-nitrophenyl esters. The resins are washed 5 times with DCM and a solution of an acyl hydrazide in DMF is added to the 4-nitrophenyl esters. After shaking overnight, the resulting resin bound diacyl hydrazides are washed with DMF, DCM and Methanol (4 times each) and dried. The resin bound diacyl hydrazides are then suspended in a solution of triethylamine (10 eq) and triphenylphosphine (10 eq) in DCM. To the solutions is added carbon tetrachloride (9 eq) dropwise over 15 minutes. The cyclization reaction is allowed to proceed overnight at 45°C. The resins are then washed with DCM and Methanol and dried to provide the resin bound 1,3,4-oxadiazole compounds.

EXAMPLE 38

Preparation of 1,3,4-Thiadiazoles

The resin bound carboxylic acids of examples 28 and 29 are placed in a solution of 4-nitrophenyl trifluoroacetate (10 equivalents) in DCM and shaken at RT for 6 hours to give the corresponding 4-nitrophenyl esters. The resins are washed 5 times with DCM and a solution of an acyl hydrazide in DMF is added to the 4-nitrophenyl esters. After shaking overnight, the resulting resin bound diacyl hydrazides are washed with DMF, DCM and Methanol (4 times each) and dried. The diacylhydrazides are suspended in a solution of Lawesson's reagent (10 eq) in toluene, and the solutions heated to 110°C overnight. The resins are then washed

with DCM, DMF, DCM and Methanol (4X each) and dried to provide the resin bound 1,3,4-thiadiazole compounds.

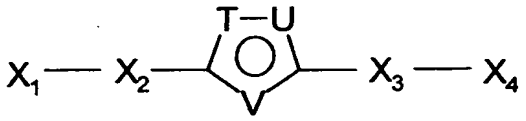
EXAMPLE 39
Preparation of 1,2,4-Triazoles

The resin bound carboxylic acids of examples 28 and 29 are placed in a solution of 4-nitrophenyl trifluoroacetate (10 equivalents) in DCM and shaken at RT for 6 hours to give the corresponding 4-nitrophenyl esters. The resins are washed 5 times with DCM and a solution of hydrazide in DMF is added to the 4-nitrophenyl esters. After shaking overnight, the resulting resin bound acyl hydrazides are washed with DMF, DCM and Methanol (4 times each) and dried. The resins are treated with a solution of an amidine (5 eq) and potassium carbonate (10 eq) in 2-methoxyethanol. The mixtures are heated at 100°C for 3 days, then the resins are washed with DMF and Methanol and dried to provide the corresponding resin bound 1,2,4-triazole compounds.

Although the invention has been described with reference to the examples provided above, it should be understood that various modifications can be made by those skilled in the art without departing from the invention. Accordingly, the invention is set out in the following claims.

WE CLAIM:

1. A single compound of the structure:

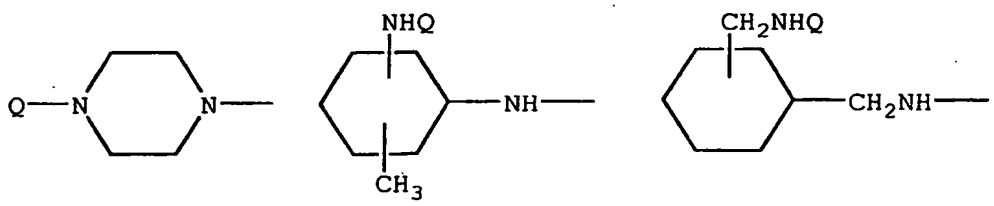


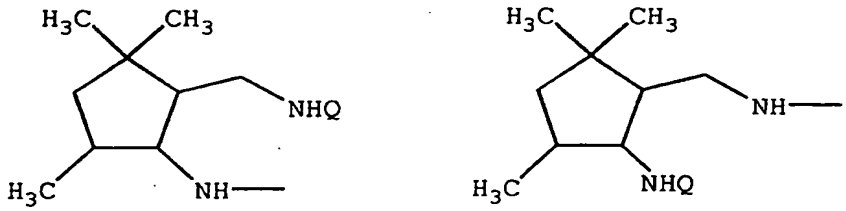
Formula (I)

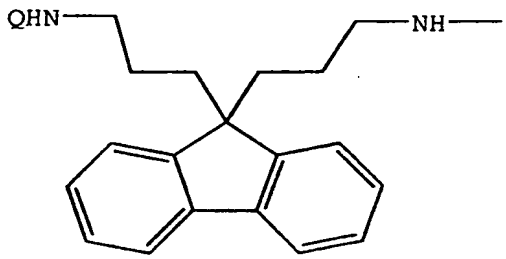
wherein:

T, U and V are independently selected from an oxygen, sulfur or nitrogen atom, provided that at least two of T, U and V are a nitrogen atom;

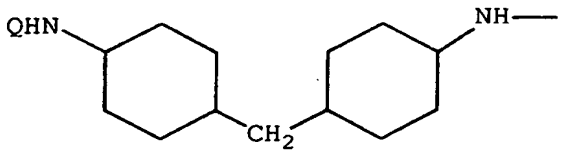
X_1 is selected from the group consisting of H, $-NHC(O)NR_1R_2$, $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$, and $-CH_2NR_1R_2$, wherein R_1 is a hydrogen atom or a functionalized resin, and R_2 is a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, the formulae:







and



wherein Q is a hydrogen atom or functionalized resin;

X_2 is selected from the group consisting of C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_2 to C_7 alkenylene, C_2 to C_7 substituted alkenylene, C_2 to C_7 alkynylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, C_5 to C_7 cycloalkenylene, C_5 to C_7 substituted cycloalkenylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, C_7 to C_{12} substituted phenylalkylene, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy,

the formula:

$$-(CH_2)_m-G-(CH_2)_n-$$

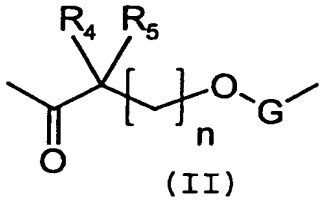
wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and G is selected from phenylene and substituted phenylene,

the formula:

$$-(CH_2)_m-NR_3-(CH_2)_n-$$

wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and R_3 is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_4 alkyl sulfonyl, C_1 to C_4 substituted alkyl sulfonyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl, substituted phenylaminothiocarbonyl, C_1 to C_7 alkoxycarbonyl, C_1 to C_7 substituted alkoxycarbonyl, phenoxycarbonyl and substituted phenoxycarbonyl,

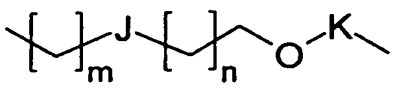
the formula:



(II)

wherein n is an integer selected from 0 to 6; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl and protected hydroxymethyl; and G is selected from phenylene and substituted phenylene, and

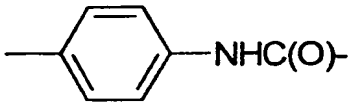
the formula:



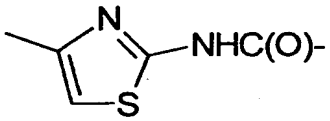
(III)

wherein J and K are each selected from the group consisting of phenylene and substituted phenylene, and m and n are independently selected from 0 and 1, and

the formulae (IV) and (V):

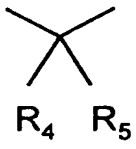


(IV)



(V) ; and

X_3 is absent or is selected from the group consisting of the formula:

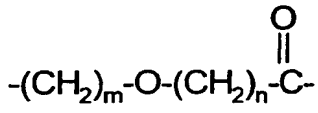


wherein:

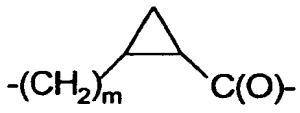
R_4 and R_5 are together or independently selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_1 to C_6 substituted

alkyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl and protected hydroxymethyl,

the formulae (VIa) and (VIb):



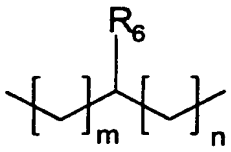
(VIa)



(VIb)

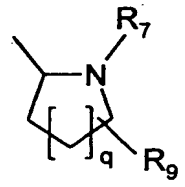
wherein in formula (VIa) m and n are independently selected from 0, 1, 2, 3 and 4; and wherein in formula (VIb) m is selected from 0, 1, 2, 3 and 4;

the formula:

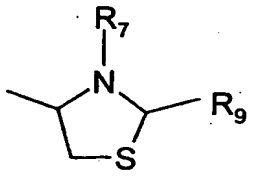


wherein R_6 is selected from the group consisitng of a hydrogen atom, amino, amino-protecting group, $-NR_7R_8$, carboxy, carboxy-protecting group, $-C(O)NR_7R_8$, wherein R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and m and n are independently selected from 0, 1, 2, 3 and 4; and

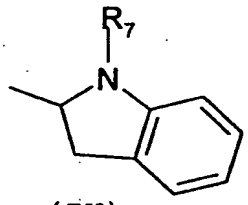
the formulae (VII) to (XIII):



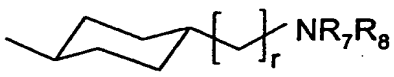
(VII)



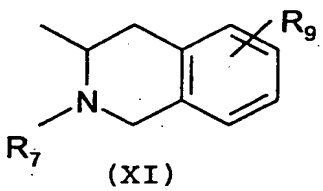
(VIII)



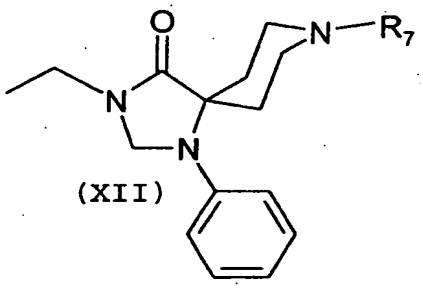
(IX)



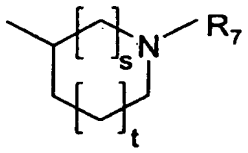
(X)



(XI)



(XII)



(XIII)

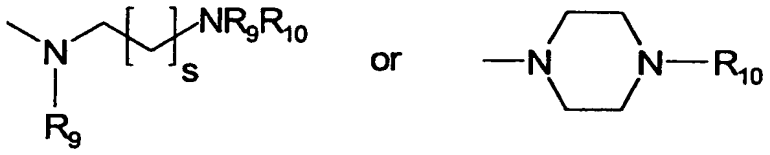
wherein q is 1 or 2; r is 0 or 1; s and t are independently selected from 0, 1 or 2; and R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl,

C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and

R_9 is selected from a hydrogen atom, -OH, hydroxy-protecting group, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 phenylalkoxy, phenyl, substituted phenyl, heteroaryl and substituted heteroaryl; and

X_4 is absent or is selected from the group consisting of a hydrogen atom, -OH, $-CO_2H$, $-C(O)NR_7R_8$ and $-NR_7R_8$, wherein R_7 and R_8 are independently selected from a functionalized resin, a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl,

and the formulae:



wherein R_9 and R_{10} are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and s is an integer selected from 1 to 5;

a pharmaceutically acceptable salt of a compound thereof; or

a biologically active ester form of a compound thereof.

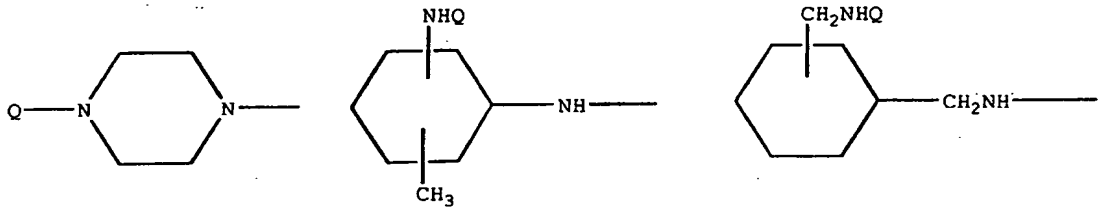
2. The single compound of claim 1, wherein one of T, U and V is oxygen and the other two positions are each nitrogen.

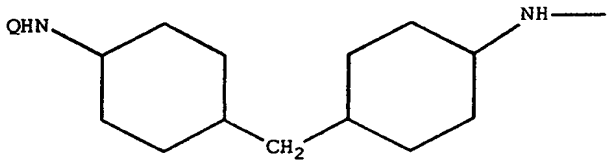
3. The single compound of claim 2, wherein U is oxygen, T is nitrogen and V is nitrogen.

4. The single compound of claim 1, wherein

X_1 is selected from the group consisitng of $-CO_2R_1$, $-OR_1$, NR_1R_2, $-C(O)NR_1R_2$,

and the formulae:



and 

;

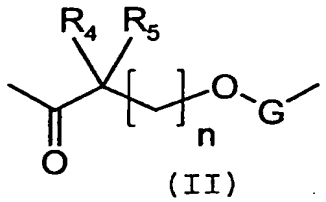
X_2 is selected from the group consisting of C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, C_7 to C_{12} substituted phenylalkylene,

the formula:

$$-(CH_2)_m-NR_3-(CH_2)_n-$$

wherein m is 1 to 3 and n is 1 to 4,

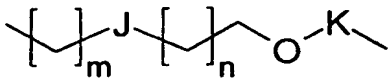
and the formula:



(II)

wherein n is 0 or 1; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl or C_1 to C_{10} substituted alkyl,

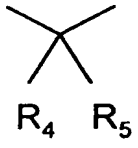
and the formula:



(III)

wherein m and n are integers independently selected from 0 and 1;

X_3 is absent or the formula:

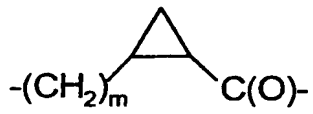


wherein:

R_4 and R_5 are together or independently selected from the group consisting of a hydrogen atom, C_1

to C_6 alkyl., C_7 to C_{12} substituted phenylalkyl, substituted phenyl, hydroxymethyl, protected hydroxymethyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl,

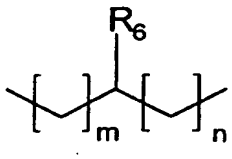
the formula:



(VIb)

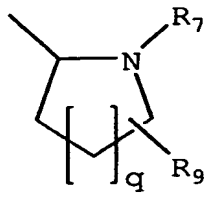
wherein m is 0,

and the formula:



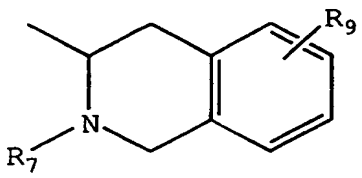
wherein m is 0 to 2 and n is 1 to 4; and

where X_3 is absent, X_4 is selected from the group consisting of the formulae:

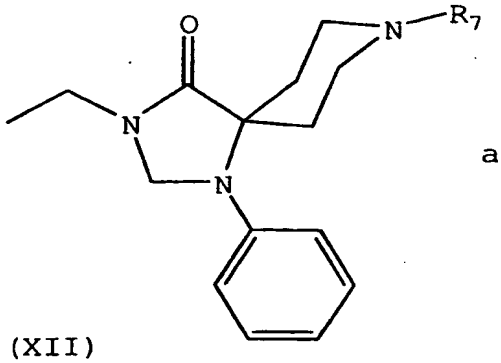


(VII)

(X)

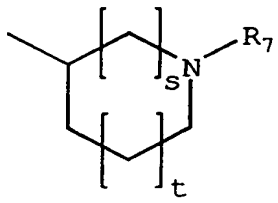


(XI)



(XII)

and



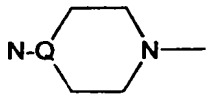
(XIII)

wherein R_9 is selected from a hydrogen atom and -OH.

5. The single compound of claim 1, wherein:

X_1 is selected from the group consisting of $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$,

and the formula:



6. The single compound of claim 3, wherein:

X_1 is selected from the group consisting of OH, $CONH_2$, 2-(1-pyrrolidino)ethylamine, 2-pyridinemethylamine, 2-(4-imidazole)ethylamine, cyclopentylamine, allylamine, 2-methoxyethylamine,

(+/-)-tetrahydrofurylamine, benzylamine, 2-methylbenzylamine, 3-methylbenzylamine, 4-methylbenzylamine, 2-fluorobenzylamine, 3-fluorobenzylamine, 4-fluorobenzylamine, 3-(1-imidazole)propylamine, 4-aminomethylbenzylamine, 4-methoxybenzylamine, 3-chlorobenzylamine, 3-bromobenzylamine, 4-bromobenzylamine, cyclopropylamine, cyclopropanemethylamine, 4-pyridinemethylamine, 3-pyridinemethylamine, 2-thiophenemethylamine, phenethylamine, 2-(morpholine)ethylamine, 3-methoxybenzylamine, piperonylamine, 4-methoxyphenethylamine, 2-fluorophenethylamine, 2-(4-chlorophenyl)ethylamine, 2-(3-chlorophenyl)ethylamine, 2-(2-chlorophenyl)ethylamine, 2,3-dimethoxybenzylamine, 3,4-dimethoxyphenethylamine, 2,4-dichlorophenethylamine, 2-(diethylamino)ethylamine, 2-(1-methylpyrrolidin-2-yl)ethylamine, 3-(diethylamino)propylamine, 2-(5-nitro-2-pyridyl)ethylamine, 3-(dimethylamino)-2,2-dimethylpropylamine, 3-(dimethylamino)propylamine, 2-aminoethylamine, 2-(piperidino)ethylamine, isoamylamine, 3-ethoxypropylamine, 3-(2-pipecolinyl)propylamine, 3-butoxypropylamine, 3-(pyrrolidin-2-one-1-yl)propylamine, 3-(morpholino)propylamine, 2-(N-ethyl-3-methylanilino)ethylamine, 3-phenyl-1-propylamine, 2-methyl-2-phenylethylamine, 4-phenylbutylamine, 3,3-diphenylpropylamine, isobutylamine, 2-(2-pyridyl)ethylamine, cyclohexanemethylamine, 3-methoxyphenethylamine, 3-phenylbenzylamine, and piperazine;

X_2 is selected from the group consisting of methylene,

1,1-cyclopropyl, 1,3-phenylene, 1,4-phenylene,
1-methyl-1-(4-oxyphenylene)ethane,
3-methoxy-1,4-phenylene, 2-fluoro-1,4-phenylene,
4,4'-biphenylene, 1,2-phenylene,
3,5-dibromo-1,4-phenylene,
4-phenyl-1-(methylene-1-yl),
3,5-diiodo-1,4-phenylene, 3-hydroxy-1,4-phenylene,
2,3,5,6-tetrafluoro-1,4-phenylene,
3-bromo-1,4-phenylene, 3,5-di-tert-
butyl-1,4-phenylene,
3,5-di-tert-butyl-4-phenyl-1-(methylene-1-yl),
3-methoxy-4-phenyl-1-(methylene-1-yl),
3-nitro-1,4-phenylene, 5-hydroxy-1,3-phenylene,
4-phenyl-1-(-2-ethyl),
3-ethoxy-4-phenyl-1-(methylene-1-yl),
2-chloro-1,4-phenylene, 2-fluoro-1,4-phenylene,
3,5-dimethyl-1,4-phenylene,
2,6-dimethyl-1,4-phenylene,
3,5-dichloro-1,4-phenylene,
3-methoxy-2-phenyl-1-(methylene-1-yl),
8-quinoline-2-yl, 5-indole-3-(methylene-1-yl),
3,hydroxy-4-phenyl-1-(methylene-1-yl),
4-chloro-1,2-phenylene, 6-nitro-1,2-phenylene,
5-nitro-1,2-phenylene,
2-amino-1,4-phenylene,2-carboxymethyl-1,4-phenylene,
3-bromo-5-methoxy-4-phenyl-1-(methylene-1-yl),
3,5-dimethoxy-4-phenyl-1-(methylene-1-yl),
2-iodo-6-nitro-1,4-phenylene;

X_3 is selected from the group consisting of
1-aminomethylene,
1-(1-aminoethyl),1-(2-aminoethyl),
1-(1-amino-2-(3-pyridyl)ethyl),
1-(1-amino-2-(2-thienyl)ethyl), 1-(1-aminopropyl),
1-(3-aminopropyl), 1-(5-aminopentyl),
1-(1-methyl-1-aminoethyl),
1-(4-aminomethylcyclohexyl),

1-(1-amino-3-guanidinopropyl), 3-(3-aminopropionic acid), 3-(2-aminopropionic acid), 3-methylene-1-phenyl-1,3,8-triazaspiro[4.5]decane-4-one, 1-(1-amino-2-(4-chlorophenyl)ethyl), 1-(1-amino-2-(cyclohexyl)ethyl), 4-(4-aminobutyric acid), 4-(2-aminobutyric acid), 1-(1-amino-2-(4-imidazolyl)ethyl), 1-(1-amino-2-methylbutyl), 4-piperidinyl, 1-(1-amino-3-methylbutyl), 3-piperidinyl, 1-(1-aminobutyl), 1-(1-amino-2-phenylethyl), 2-piperidinyl, 2-pyrrolidinyl, 1-(1-amino-2-hydroxyethyl), 4-thiazolidinyl, 1-(1-amino-2-hydroxypropyl), 3-tetrahydroisoquinolinyl, 1-(1-amino-2-(3-indolyl)ethyl), 1-(1-amino-2-(4-hydroxyphenyl)ethyl), 1-(1-amino-2-(4-ethoxyphenyl)ethyl), 1-(1-amino-2-methylpropyl), 1-(1,5-diaminopentyl), 2-(1-pyrrolidino)ethylaminomethylene, 2-pyridinemethylaminomethylene, 2-(4-imidazole)ethylaminomethylene, cyclopentylaminomethylene, allylaminomethylene, 2-methoxyethylaminomethylene, (+/-)-tetrahydrofurylaminomethylene, benzylaminomethylene, 2-methylbenzylaminomethylene, 3-methylbenzylaminomethylene, 4-methylbenzylaminomethylene, 2-fluorobenzylaminomethylene, 3-fluorobenzylaminomethylene, 4-fluorobenzylaminomethylene, 3-(1-imidazole)propylaminomethylene, 4-aminomethylbenzylaminomethylene, 4-methoxybenzylaminomethylene, 3-chlorobenzylaminomethylene, 3-bromobenzylaminomethylene, 4-bromobenzylaminomethylene, cyclopropylaminomethylene,

cyclopropanemethylaminomethylene,
4-pyridinemethylaminomethylene,
3-pyridinemethylaminomethylene,
2-thiophenemethylaminomethylene,
phenethylaminomethylene,
2-(morpholine)ethylaminomethylene, 3-methoxybenzylaminomethylene,
piperonylaminomethylene,
4-methoxyphenethylaminomethylene,
2-fluorophenethylaminomethylene,
2-(4-chlorophenyl)ethylaminomethylene,
2-(3-chlorophenyl)ethylaminomethylene,
2-(2-chlorophenyl)ethylaminomethylene,
2,3-dimethoxy- benzylaminomethylene,
3,4-dimethoxyphenethylaminomethylene, 2,4-dichlorophenethylaminomethylene,
2-(diethylamino)ethylaminomethylene,
2-(1-methylpyrrolidin-2-yl)ethylaminomethylene,
3-(diethylamino)propylaminomethylene,
2-(5-nitro-2-pyridyl)ethylaminomethylene,
3-(dimethylamino)-2,2-dimethylpropylaminomethylene,
3-(dimethylamino)propylaminomethylene,
2-aminoethylaminomethylene,
2-(piperidino)ethylaminomethylene,
isoamylaminomethylene, 3-ethoxypropylaminomethylene,
3-(2-pipecolinyl)propylaminomethylene,
3-butoxypropylaminomethylene,
3-(pyrrolidin-2-one-1-yl)propylaminomethylene,
3-(morpholino)propylaminomethylene,
2-(N-ethyl-3-methylanilino)ethylaminomethylene,
3-phenyl-1- propylaminomethylene,
2-methyl-2-phenylethylaminomethylene,
4-phenylbutylaminomethylene,
3,3-diphenylpropylaminomethylene,
isobutylaminomethylene,
2-(2-pyridyl)ethylaminomethylene,
cyclohexanemethylaminomethylene,

3-methoxyphenethylaminomethylene,
3-phenylbenzylaminomethylene, and
piperazinomethylene; and

X_4 is selected from the group consisting of acetyl, alpha-methylcinnamyl, benzoyl, crotonyl, cyclobutanecarbonyl, cyclohexanepropionyl, 4-cyanobenzoyl, hydrocinnamyl, 4-dimethylaminobenzoyl, 4-ethoxybenzoyl, isobutyryl, 4- ethoxyphenylacetyl, isovaleryl, levulinyl, m-anisyl, m-toluyl, methoxyacetyl, isonicotinyl, p-tolylacetyl, picolinyl, piperonylyl, 4-fluoro-alpha- methylphenylacetyl, 4-fluorophenylacetyl, tetrahydro-3-furoyl, trans-3-(3-pyridyl)acrylyl, trimethylacetyl, triphenylacetyl, nicotinyl, (3,4-dimethoxyphenyl)acetyl, boc-isonipecotyl, (alpha-alpha-alpha-trifluoro-m-tolyl)acetyl, (methylthio)acetyl, (phenylthio)acetyl, 1-(4-chlorophenyl)-1- cyclopentanecarbonyl, 1-adamantaneacetyl, 1-naphthylacetyl, 1-phenyl-1-cyclopropanecarbonyl, 4-iodobenzoyl, 4-isopropoxybenzoyl, 2,4-dichlorobenzoyl, 4-methyl-1-cyclohexanecarbonyl, pyrrole-2- carbonyl, 4-methylvaleryl, 1- naphthylacetyl, 2-fluorobenzoyl, 1,3-phenylene diacetyl, 2-norbornaneacetyl, 2-pyrazinecarbonyl, 2-pyridylacetyl, 2-thiopheneacetyl, 3,4,5- triethoxybenzoyl, 3,4-methylenedioxyphenylacetyl, 3,4-dichlorobenzoyl, 4- isopropylbenzoyl, 3,4-dichlorophenylacetyl, 4-tert-butyl-cyclohexanecarbonyl, 4-sulfonamidobenzoyl, 3,5,5-trimethylhexanoyl, 3,5-bis(trifluoromethyl)-benzoyl, 5-bromo-2-chlorobenzoyl, 5-bromonicotinyl, 6-chloronicotinyl, 3,5-dimethyl-p-anisyl, 3-bromo-4-methylbenzoyl, 3,4,5-trimethoxyphenylacetyl, 3-benzoylpropionyl,

3,5-dichlorobenzoyl, 3-cyanobenzoyl,
3-fluoro-4-methylbenzoyl, 1-isoquinolinecarbonyl,
3-methyl-2-thiophenecarbonyl, 3-phenoxybenzoyl,
3-thiopheneacetyl, 4- biphenylacetyl,
4-bromophenylacetyl, s-(+)-mandelyl,
3,5-di-tert-butyl-4-hydroxybenzoyl,
3,5-dichloro-4-hydroxybenzoyl, 4- hydroxybenzoyl,
5-methylsalicylyl, 2- methylcyclopropanecarbonyl,
3-lndolepropionyl, 2,2-diphenylacetyl,
5-methoxyindole-2-carbonyl, succinamyl,
4-dimethylaminobutyryl, 4- methylthiobenzoyl,
2-methylthionicotinyl,
r(-)-2-oxothiazolidine-4-carbonyl,
4-nitrophenylacetyl, coumarin-3-carbonyl,
1-cyano-1-cyclopropane carbonyl,
2-chloro-5-(methylthio)benzoyl,
theophylline-7-acetyl, 2-(2-cyanophenylthio)benzoyl,
2-mesitylenesulfonyl, 2-naphthalenesulfonyl,
2-thiophenesulfonyl, 4-chlorobenzenesulfonyl,
4-fluorobenzenesulfonyl, 4-methoxybenzenesulfonyl,
4-methylsulfonylbenzenesulfonyl, benzenesulfonyl,
dansyl, n-acetylsulfanilyl,
2-acetamido-4-methyl-5-thiazolesulfonyl, 4-
(trifluoromethoxy)benzenesulfonyl,
4-tert-butylbenzenesulfonyl, 8-quinolinesulfonyl,
2,3-dichlorothiophene-5-sulfonyl,
3,4-dimethoxybenzenesulfonyl, 3,5-
bis(trifluoromethyl)benzenesulfonyl,
3-chloro-4-fluorobenzenesulfonyl,
3-trifluoromethylbenzenesulfonyl,
4-ethylbenzenesulfonyl, pentamethylbenzenesulfonyl,
2,3,4-trifluorobenzenesulfonyl,
2,4-dichlorobenzenesulfonyl,
2,5-dichlorothiophene-3-sulfonyl,
2,6-dichlorobenzenesulfonyl,
2,6-difluorobenzenesulfonyl,
2-chloro-4-(trifluoromethyl)benzenesulfonyl,

2-chloro-5-(trifluoromethyl)benzenesulfonyl, 2-chloro-6-methylbenzenesulfonyl, 3,4-difluorobenzenesulphonyl, 3,5-dichlorobenzenesulfonyl, 3-chlorobenzenesulfonyl, 4-(n- butoxy)benzenesulfonyl, 4-trifluoromethylbenzene sulfonyl, 3,5-dimethylisoxazole-4-sulfonyl, 2-(methoxycarbonyl)thiophene-3-sulfonyl, 4-acetamido-3-chlorobenzene sulfonyl, 2-[1-methyl-5-(trifluoromethyl)pyrazol-3-yl]thiophene-5-sulfonyl, 2-(benzoylaminomethyl)thiophene-5-sulfonyl, 3-methoxy-4-(methoxycarbonyl)-thiophene-2-sulfonyl, 5-(isoxazol-3- yl)thiophene-2-sulfonyl, 4-cyanobenzene sulfonyl, 3-chloro-4-methylbenzenesulfonyl, 2,4-difluorobenzenesulfonyl, 2-fluorobenzenesulfonyl, 4-isopropylbenzene sulfonyl, 2,5-dimethoxybenzenesulfonyl, 3,4-dichlorobenzenesulfonyl, (2s,3s)-2-(carbamyl)-3-methylvalerate methyl ester, (r)-(-)-1-(carbamyl)-(1-naphthyl)ethane, (s)-(+)-1-(carbamyl)-(1-naphthyl)ethane, (s)-(+)-2-(carbamyl)-3-tert-butoxypropionate methyl ester, (s)-(-)-2-(carbamyl)-3-methylbutyrate methyl ester, (s)-(-)-2-(carbamyl)-4-(methylthio)butyrate methyl ester, (s)-(-)-2-(carbamyl)-4-methylvalerate methyl ester, (s)-(-)-2-(carbamyl)glutarate diethyl ester, (s)-(-)-2-(carbamyl)propionate methyl ester, (s)-2-(carbamyl)-3- phenylpropionate methyl ester, 1-(carbamyl)-tridecafluoro-1-hexane, 1-(carbamyl)-1,1,3,3-tetramethylbutane, 1-(carbamyl)-(1-naphthyl)ethane, 1-(carbamyl)-(4-bromophenyl)ethane, 1-(carbamyl)-adamantane, 1-(carbamyl)naphthalene, 1-(carbamyl)-2,3,4-trifluorobenzene, 1-(carbamyl)-2,3-dichlorobenzene,

1-(carbamyl)-2,3-dimethylbenzene,
1-(carbamyl)-2,4,5-trichlorobenzene,
1-(carbamyl)-2,4,5-trimethylbenzene,
1-(carbamyl)-2,4,6-trichlorobenzene,
1-(carbamyl)-2,4-dichlorobenzene, 1-(carbamyl)-2,4-difluorobenzene, 1-(carbamyl)-2,4-dimethoxybenzene,
1-(carbamyl)-2,4-dimethylbenzene,
1-(carbamyl)-2,5-dichlorobenzene,
1-(carbamyl)-2,5-difluorobenzene,
1-(carbamyl)-2,5-dimethoxybenzene, 1-(carbamyl)-2,5-dimethylbenzene,
1-(carbamyl)-2,6-dibromo-4-fluorobenzene,
1-(carbamyl)-2,6-dibromo-4-isopropylbenzene,
1-(carbamyl)-2,6-dichlorobenzene,
1-(carbamyl)-2,6-diethylbenzene,
1-(carbamyl)-2,6-difluorobenzoyl,
1-(carbamyl)-2,6-difluorobenzene,1-(carbamyl)-2,6-diisopropylbenzene, 1-(carbamyl)-2,6-dimethylbenzene,
1-(carbamyl)-2-(chloromethyl)benzene,
1-(carbamyl)-2-(difluoromethoxy)benzene,
1-(carbamyl)-2-(methylthio)benzene,
1-(carbamyl)-2-(trifluoromethoxy)benzene,
1-(carbamyl)-2-(trifluoromethyl)benzene,
1-(carbamyl)-2-biphenyl,
1-(carbamyl)-2-bromo-4,6-difluorobenzene,
1-(carbamyl)-2-bromoethane,
1-(carbamyl)-2-bromobenzene,
1-(carbamyl)-2-chloro-4-nitrobenzene,
1-(carbamyl)-2-chloro-5-(trifluoromethyl)benzene,
1-(carbamyl)-2-chloro-5- nitrobenzene,
1-(carbamyl)-2-chloro-6-methylbenzene,
1-(carbamyl)-2-chlorobenzyl,
1-(carbamyl)-2-chloroethane,
1-(carbamyl)-2-chlorobenzene,
1-(carbamyl)-2-cyanobenzene,
1-(carbamyl)-2-ethoxybenzene,
1-(carbamyl)-2-ethyl-6-methylbenzene,

1-(carbamyl)-2-ethylbenzene,
1-(carbamyl)-2-fluoro-3-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluoro-5-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluoro-5-methylbenzene,
1-(carbamyl)-2-fluoro-5-nitrobenzene,
1-(carbamyl)-2-fluoro-6-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluorobenzene,
1-(carbamyl)-2-iodobenzene,
1-(carbamyl)-2-isopropyl-6-methylbenzene,
1-(carbamyl)-2-isopropylbenzene,
1-(carbamyl)-2-methoxy-5-chloro benzene,
1-(carbamyl)-2-methoxy-5-methylbenzene,
1-(carbamyl)-2-methoxy-5-nitrobenzene,
1-(carbamyl)-2-methoxybenzene,
1-(carbamyl)-2-methyl-3-nitrobenzene,
1-(carbamyl)-2-methyl-5-nitrobenzene,
1-(carbamyl)-2-methyl-6-t-butylbenzene,
1-(carbamyl)-1-(2-methylphenyl)methane,
1-(carbamyl)-2-n-propylbenzene,
1-(carbamyl)-2-naphthalene,
1-(carbamyl)-2-nitrobenzene,
1-(carbamyl)-2-phenoxybenzene,
1-(carbamyl)-2-tert-butylbenzene,
1-(carbamyl)-3,4,5-trimethoxybenzene,
1-(carbamyl)-1-(3,4-dichlorophenyl)methane,
1-(carbamyl)-3,4-dichlorobenzene,
1-(carbamyl)-3,4-difluorobenzene,
1-(carbamyl)-3,4-dimethylbenzene,
1-(carbamyl)-3,5-bis(trifluoromethyl)benzene,
1-(carbamyl)-3,5- dichlorobenzene,
1-(carbamyl)-3,5-dimethoxybenzene,
1-(carbamyl)-3,5-dimethylbenzene, 1-(carbamyl)-3,5-dinitrobenzene, 1-(carbamyl)-3-(methylthio)benzene,
1-(carbamyl)-3-(trifluoromethyl)benzene,
1-(carbamyl)-3-(trifluoromethylthio)benzene,
1-(carbamyl)-3-acetylbenzene,
1-(carbamyl)-3-bromobenzene,

1-(carbamyl)-3-bromopropane,
1-(carbamyl)-3-carbomethoxybenzene,
1-(carbamyl)-3-chloro-2-methoxybenzene,
1-(carbamyl)-3-chloro-2-methylbenzene,
1-(carbamyl)-3-chloro-4-fluorobenzene,
1-(carbamyl)-3-chloro-4-methylbenzene,
1-(carbamyl)-3-chlorobenzene,
1-(carbamyl)-3-chloropropane,
1-(carbamyl)-3-cyanobenzene,
1-(carbamyl)-3-cyclopentoxy-4-methoxybenzene,
1-(carbamyl)-3-ethylbenzene,
1-(carbamyl)-3-fluoro-4-methylbenzene,
1-(carbamyl)-3-fluorobenzene,
1-(carbamyl)-3-iodopropane, 3-(carbamyl)benzoyl chloride, 1-(carbamyl)-3-methoxybenzene,
1-(carbamyl)-(3-methylphenyl)methane,
1-(carbamyl)-3-nitrobenzene,
1-(carbamyl)-3-pyridine,
4'-(carbamyl)-5'-nitrobenzo-15-crown-5,
4'-(carbamyl)benzo-15-crown-5,
4'-(carbamyl)benzo-18-crown-6,
1-(carbamyl)-4,5-dimethyl-2-nitrobenzene,
1-(carbamyl)-4-(6-methyl-2-benzothiazolyl)benzene,
1-(carbamyl)-4-(chloromethyl)benzene,
1-(carbamyl)-4-(chlorosulfonyl)benzene,
1-(carbamyl)-4-(difluoromethoxy)benzene,
1-(carbamyl)-4-(methylthio)benzene,
1-(carbamyl)-4-(tert-butyl)benzene,
1-(carbamyl)-4-(trifluoromethoxy)benzene,
1-(carbamyl)-4-(trifluoromethyl)benzene,
1-(carbamyl)-4-(trifluoromethylthio)benzene,
1-(carbamyl)-4-acetylbenzene,
1-(carbamyl)-4-benzyloxybenzene,
1-(carbamyl)-4-bromo-2,6-dimethylbenzene,
1-(carbamyl)-4-bromo-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-bromo-2-chlorobenzene,
1-(carbamyl)-4-bromo-2-fluorobenzene,

1-(carbamyl)-4-bromo-2-methylbenzene,
1-(carbamyl)-4-bromobenzene,
1-(carbamyl)-4-chloro-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-chloro-2-methoxybenzene,
1-(carbamyl)-4-chloro-2-methylbenzene,
1-(carbamyl)-4-chloro-2-nitrobenzene,
1-(carbamyl)-4-chloro-3-(trifluoromethyl)benzene,
1-(carbamyl)-4-chloro-3-nitrobenzene,
1-(carbamyl)-4-chlorobenzene,
1-(carbamyl)-4-dimethylaminobenzene,
1-(carbamyl)-4-ethoxybenzene,
1-(carbamyl)-4-ethylbenzene,
1-(carbamyl)-4-fluoro-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-fluoro-2-nitrobenzene,
1-(carbamyl)-4-fluoro-3-(trifluoromethyl)benzene,
1-(carbamyl)-4-fluoro-3-nitrobenzene,
1-(carbamyl)-4-fluorobenzoyl,
1-(carbamyl)-4-fluorobenzyl,
1-(carbamyl)-4-fluorobenzene,
1-(carbamyl)-4-heptyloxybenzene,
1-(carbamyl)-4-iodobenzene, 4-(carbamyl)benzoyl chloride, 1-(carbamyl)-4-isopropylbenzene,
1-(carbamyl)-4-methoxy-2-methylbenzene,
1-(carbamyl)-(4-methoxyphenyl)methane,
1-(carbamyl)-4-methoxybenzene,
1-(carbamyl)-4-methyl-2-nitrobenzene,
1-(carbamyl)-4-methyl-3-nitrobenzene,
1-(carbamyl)-(4-methylphenyl)methane,
1-(carbamyl)-4-n-butoxycarbonylbenzene,
1-(carbamyl)-4-n-butoxybenzene,
1-(carbamyl)-4-n-butyl-2-methylbenzene,
1-(carbamyl)-4-n-butylbenzene,
1-(carbamyl)-4-nitrobenzene,
1-(carbamyl)-4-phenoxybenzene,
1-(carbamyl)-5-bromopenane,
1-(carbamyl)-5-chloro-2,4-dimethoxybenzene,
1-(carbamyl)-5-chloro-2-methylbenzene,

1-(carbamyl)-5-fluoro-2-methylbenzene,
1-(carbamyl)-5-iodopentane, 1-(carbamyl)-2-propene,
benzoyl carbamyl, 1-(carbamyl)-1-phenylmethane,
1-(carbamyl)-cyclohexane, carboxyethylcarbamyl,
ethyl 2-(carbamyl)-3-methylbutyrate, ethyl
2-(carbamyl)-3-phenylpropionate, ethyl
2-(carbamyl)-4- (methylthio)butyrate, ethyl
2-(carbamyl)-4-methylvalerate, ethyl
2-(carbamyl)benzoate, ethyl 2-(carbamyl)propionate,
ethyl 3-(carbamyl)benzoate, ethyl
3-(carbamyl)propionate, ethyl 4-(carbamyl)-benzoate,
ethyl 6-(carbamyl)hexanoate, 1-(carbamyl)-ethyl,
ethyl(carbamyl)acetate, 1-(carbamyl)-heptane,
1-(carbamyl)-hexane, 1-(carbamyl)-2-methylpropane,
1-(carbamyl)ethyl methacrylate,
1-(carbamyl)-2-methylethane, methyl
2-(carbamyl)benzoate, carbamylmethane,
methyl(carbamyl)propionate, 1-(carbamyl)butane,
n-butyl (carbamyl)acetate, 1-(carbamyl)-propane,
1-(carbamyl)-pentane, 1-(carbamyl)-phenylthane,
1-(carbamyl)-benzene,
1-(carbamyl)-2,2-dimethylpropane,
1-(carbamyl)-tetrahydro-2-pyran,
1-(carbamyl)-trans-2-benzenecyclopropane,
1-(carbamyl)-trichloroacetate,
carbamyltrichloromethane,
1-(thiocarbamyl)-(2-methoxy-5-phenyl)benzene,
1-(thiocarbamyl)adamantane,
1-(thiocarbamyl)naphthalenemethane,
(thiocarbamyl)naphthalene,
1-(thiocarbamyl)2,2-diphenylethane,
1-(thiocarbamyl)-2,3,4,5-tetrachlorobenzene,
1-(thiocarbamyl)-2,3,4-trichlorobenzene,
1-(thiocarbamyl)-(2,3,4-trimethoxyphenyl)methane,
1-(thiocarbamyl)-2,3,5,6-tetrachlorobenzene,
1-(thiocarbamyl)-2,3,5,6-tetrafluorobenzene,
1-(thiocarbamyl)-2,3-dibromopropane,

1-(thiocarbamyl)-2,3-dichlorobenzene,
1-(thiocarbamyl)-(2,3-dimethoxyphenyl)methane,
1-(thiocarbamyl)-2,3-dimethylbenzene,
1-(thiocarbamyl)-2,4,5-trichlorobenzene,
1-(thiocarbamyl)-2,4,6-tribromobenzene,
1-(thiocarbamyl)-2,4,6-trichlorobenzene,
1-(thiocarbamyl)-2,4,6-trifluorobenzene,
1-(thiocarbamyl)-2,4,6-trimethylbenzene,
1-(thiocarbamyl)-2,4-dichlorobenzene,
1-(thiocarbamyl)-2,4-difluorobenzene,
1-(thiocarbamyl)-2,4-dimethoxybenzene,
1-(thiocarbamyl)-2,4-dimethylbenzene,
1-(thiocarbamyl)-2,5-dibromobenzene,
1-(thiocarbamyl)-2,5-dichlorobenzene,
1-(thiocarbamyl)-2,5-difluorobenzene,
1-(thiocarbamyl)-2,5-dimethoxybenzene,
1-(thiocarbamyl)-2,5-dimethylbenzene,
1-(thiocarbamyl)-2,6-dichlorobenzene,
1-(thiocarbamyl)-2,6-diethylbenzene,
1-(thiocarbamyl)-2,6-difluorobenzene,
1-(thiocarbamyl)-2,6-diisopropylbenzene,
1-(thiocarbamyl)-2,6-dimethylbenzene,
1-(thiocarbamyl)-2-(3,4-dimethoxyphenyl)ethane,
1-(thiocarbamyl)-2-(4-chlorophenyl)ethane,
1-(thiocarbamyl)-2-(methylthio)benzene,
1-(thiocarbamyl)-2-(trifluoromethoxy)benzene,
1-(thiocarbamyl)-2-(trifluoromethyl)benzene,
1-(thiocarbamyl)-2-bromo-4-methylbenzene,
1-(thiocarbamyl)-2-bromoethane,
1-(thiocarbamyl)-2-bromobenzene,
1-(thiocarbamyl)-2-chloro-4-methylbenzene,
1-(thiocarbamyl)-2-chloro-4-nitrobenzene,
1-(thiocarbamyl)-2-chloro-5-(trifluoromethyl)benzene
, 1-(thiocarbamyl)-2-chloro-5-nitrobenzene,
1-(thiocarbamyl)-2-chloro-6-methylbenzene,
1-(thiocarbamyl)-(2-chlorophenyl)methane,
1-(thiocarbamyl)-2-chloroethane,

1-(thiocarbamyl)-2-chlorobenzene,
1-(thiocarbamyl)-2-cyanobenzene,
1-(thiocarbamyl)-2-ethoxycarbonylbenzene,
1-(thiocarbamyl)-2-ethoxybenzene,
1-(thiocarbamyl)-2-ethyl-6-(1-methylpropyl)benzene,
1-(thiocarbamyl)-2-ethyl-6-isopropylbenzene,
1-(thiocarbamyl)-2-ethyl-6-methylbenzene,
1-(thiocarbamyl)-2-ethylbenzene,
1-(thiocarbamyl)-(2-fluorophenyl)methane,
1-(thiocarbamyl)-2-fluoroethane,
1-(thiocarbamyl)-2-fluorobenzene,
2-(thiocarbamyl)furan, 2-(thiocarbamyl)hexane,
1-(thiocarbamyl)-2-iodobenzene,
1-(thiocarbamyl)-2-isopropyl-6-methylbenzene,
1-(thiocarbamyl)-2-isopropylbenzene,
1-(thiocarbamyl)-2-methoxy-4-nitrobenzene,
1-(thiocarbamyl)-2-methoxy-5-methylbenzene,
1-(thiocarbamyl)-2-methoxy-5-nitrobenzene,
1-(thiocarbamyl)-(2-methoxyphenyl)methane,
1-(thiocarbamyl)-2-methoxyethane,
1-(thiocarbamyl)-2-methoxybenzene,
1-(thiocarbamyl)-2-methyl-4-nitrobenzene,
1-(thiocarbamyl)-2-methyl-5-nitrobenzene,
1-(thiocarbamyl)-(2-methylphenyl)methane,
1-(thiocarbamyl)-2-methylbutane,
1-(thiocarbamyl)-2-(morpholino)ethane,
2-(thiocarbamyl)-naphthalene,
2-(thiocarbamyl)pentane,
1-(thiocarbamyl)-2-phenylethane,
1-(thiocarbamyl)-2-piperidinoethane,
2-(thiocarbamylmethyl)-tetrahydrofuran,
1-(thiocarbamyl)-3,4,5-trimethoxybenzene,
1-(thiocarbamyl)-3,4-(ethylenedioxy)benzene,
1-(thiocarbamyl)-3,4-dichlorophenyl)methane,
1-(thiocarbamyl)-3,4-dichlorobenzene,
1-(thiocarbamyl)-(3,4-dimethoxyphenyl)methane,
1-(thiocarbamyl)-3,4-dimethoxybenzene,

1-(thiocarbamyl)-3,4-dimethylbenzene,
1-(thiocarbamyl)-(3,4-methylenedioxyphenyl)methane,
1-(thiocarbamyl)-3,4-methylenedioxybenzene,
1-(thiocarbamyl)-3,5-bis(trifluoromethyl)benzene,
1-(thiocarbamyl)-3,5-dichlorobenzene,
1-(thiocarbamyl)-3,5-dimethoxybenzene,
1-(thiocarbamyl)-3,5-dimethylbenzene,
1-(thiocarbamyl)-3-(diethylamino)propane,
1-(thiocarbamyl)-3-(methylthio)benzene,
1-(thiocarbamyl)-3-(trifluoromethyl)benzene,
1-(thiocarbamyl)-3-acetylbenzene,
1-(thiocarbamyl)-3-benzyloxybenzene,
1-(thiocarbamyl)-3-bromobenzene,
1-(thiocarbamyl)-3-bromopropane,
1-(thiocarbamyl)-3-carboxybenzene,
1-(thiocarbamyl)-3-chloro-2-methylbenzene,
1-(thiocarbamyl)-3-chloro-4-fluorobenzene,
1-(thiocarbamyl)-(3-chloro-4-methylphenyl)methane,
1-(thiocarbamyl)-3-chloro-4-methylbenzene,
1-(thiocarbamyl)-(3-chlorophenyl)methane,
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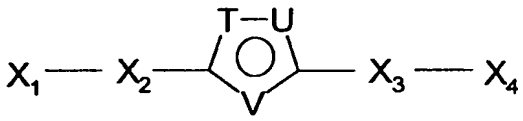
1-(thiocarbamyl)-3-chloropropane,
1-(thiocarbamyl)-3-cyanobenzene,
1-(thiocarbamyl)-3-dimethylaminopropane,
1-(thiocarbamyl)-3-ethoxycarbonylbenzene,
1-(thiocarbamyl)-3-ethylbenzene,
1-(thiocarbamyl)-(3-fluorophenyl)methane,
1-(thiocarbamyl)-3-fluorobenzene,
1-(thiocarbamyl)-3-iodobenzene,
1-(thiocarbamyl)-(3-methoxyphenyl)methane,
1-(thiocarbamyl)-3-methoxycarbonylbenzene,
1-(thiocarbamyl)-3-methoxybenzene,
1-(thiocarbamyl)-3-methoxypropane,
1-(thiocarbamyl)-3-methyl-2-butane,
1-(thiocarbamyl)-(3-methylphenyl)methane,
1-(thiocarbamyl)-3-methylbutane,
1-(thiocarbamyl)-3-morpholinopropane,

1-(thiocarbamyl)-3-nitrobenzene,
1-(thiocarbamyl)-3-pentane,
1-(thiocarbamyl)-3-phenylpropane,
3-(thiocarbamyl)pyridine,
1-(thiocarbamyl)-4-(benzyloxy)benzene,
1-(thiocarbamyl)-4-(dimethylamino)benzene,
1-(thiocarbamyl)-4-(methylthio)benzene,
1-(thiocarbamyl)-4-(trifluoromethoxy)benzene,
1-(thiocarbamyl)-4-(trifluoromethyl)benzene,
1-(thiocarbamyl)-4-acetylbenzene,
1-(thiocarbamyl)-4-bromo-2,6-dimethylbenzene,
1-(thiocarbamyl)-4-bromo-2-chlorobenzene,
1-(thiocarbamyl)-4-bromo-2-methylbenzene,
1-(thiocarbamyl)-4-bromo-2-trifluoromethylbenzene,
1-(thiocarbamyl)-4-bromobenzene,
1-(thiocarbamyl)-4-carboxybenzene,
1-(thiocarbamyl)-4-chloro-2-(trifluoromethyl)benzene
, 1-(thiocarbamyl)-4-chloro-2-methylbenzene,
1-(thiocarbamyl)-4-chloro-3-nitrobenzene,
1-(thiocarbamyl)-4-chloro-3-trifluoromethylbenzene,
1-(thiocarbamyl)-(4-chlorophenyl)methane,
1-(thiocarbamyl)-4-chlorobenzene,
1-(thiocarbamyl)-4-cyanobenzene,
1-(thiocarbamyl)-4-diethylaminobenzene,
1-(thiocarbamyl)-4-ethoxycarbonylbenzene,
1-(thiocarbamyl)-4-ethoxybenzene,
1-(thiocarbamyl)-4-ethylbenzene,
1-(thiocarbamyl)-4-fluoro-2-methylbenzene,
1-(thiocarbamyl)-(4-fluorophenyl)ethane ,
1-(thiocarbamyl)-(4-fluorophenyl)methane,
1-(thiocarbamyl)-4-fluorobenzene,
1-(thiocarbamyl)-4-iodobenzene,
1-(thiocarbamyl)-4-isopropylbenzene,
1-(thiocarbamyl)-4-methoxy-2-methylbenzene,
1-(thiocarbamyl)-4-methoxy-2-nitrobenzene,
1-(thiocarbamyl)-(4-methoxyphenyl)methane,
1-(thiocarbamyl)-4-methoxycarbonylbenzene,

1-(thiocarbamyl)-4-methoxybenzene,
1-(thiocarbamyl)-4-methyl-2-nitrobenzene,
1-(thiocarbamyl)-(4-methylphenyl)methane,
1-(thiocarbamyl)-4-n-butyl-2-methylbenzene,
1-(thiocarbamyl)-4-n-butylbenzene,
1-(thiocarbamyl)-4-nitrobenzene,
1-(thiocarbamyl)-4-phenoxybenzene,
1-(thiocarbamyl)-4-phenylazobenzene,
1-(thiocarbamyl)-4-phenylbutane,
1-(thiocarbamyl)-4-sulfamoylbenzene,
1-(thiocarbamyl)-4-tert-butylbenzene,
1-(thiocarbamyl)-5-chloro-2,4-dimethoxybenzene,
1-(thiocarbamyl)-5-chloro-2-methoxybenzene,
1-(thiocarbamyl)-5-chloro-2-methylbenzene,
1-(thiocarbamyl)-5-fluoro-2-methylbenzene,
1-(thiocarbamyl)-5-indane,
2-(thiocarbamyl)-5-norbornene,
2-(thiocarbamyl)-6-methylheptane,
9-(thiocarbamyl)acridine,
1-(thiocarbamyl)-2-propene,
1-(thiocarbamyl)-(1-phenyl)ethane,
1-(thiocarbamyl)-phenylmethane,
1-(thiocarbamyl)-cycloheptane,
1-(thiocarbamyl)-cyclohexylmethane,
1-(thiocarbamyl)-cyclohexane,
1-(thiocarbamyl)-cyclooctane,
1-(thiocarbamyl)-cyclopentane,
1-(thiocarbamyl)-cyclopropane, diethyl
L-2-thiocarbamyl-glutarate, dimethyl
L-thiocarbamyl-succinate, ethyl
2-thiocarbamylpropionate, ethyl
3-thiocarbamylbutyrate, ethyl
3-thiocarbamylpropionate, ethyl
4-thiocarbamylbutyrate, 1-(thiocarbamyl)-ethane,
ethyl thiocarbamylacetate,
1-(thiocarbamyl)-2-methylpropane,
1-(thiocarbamyl)-1-methylethane,

thiocarbamylacetaldehyde dimethyl acetal,
thiocarbamylphenyl sulfone,
1-(thiocarbamyl)-2-butene,
1-(thiocarbamyl)-methoxymethane, methyl
2-thiocarbamylacetate, methyl
2-thiocarbamylbenzoate, methyl
3-thiocarbamylpropionate,methyl
2-thiocarbamylbutyrate, methyl, methyl
L-2-thiocarbamyl-3-methyl-butyrate, methyl
L-2-thiocarbamyl-3-phenyl-propionate, methyl
L-2-thiocarbamyl-4-(methylthio)butyrate, methyl
L-2-thiocarbamyl-4-methylvalerate,
1-(thiocarbamyl)-pentane, 1-(thiocarbamyl)-butane,
1-(thiocarbamyl)-hexane, 1-(thiocarbamyl)-propane,
2-(thiocarbamyl)-norbornane,
1-(thiocarbamyl)-4-vinylbenzene,
1-(thiocarbamyl)-pentafluorobenzene,
1-(thiocarbamyl)-benzene, 1-(thiocarbamyl)-propyne
and 2-(thiocarbamyl)-butane.

7. A combinatorial library of two or more compounds of the structure:

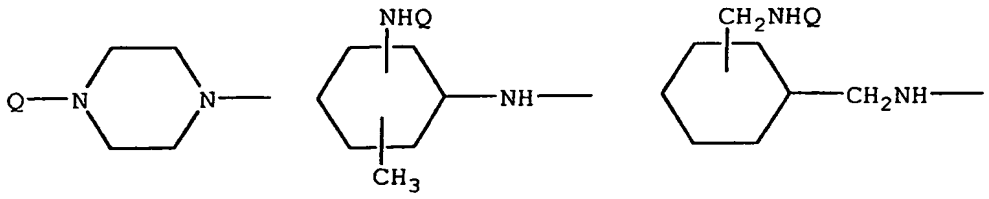


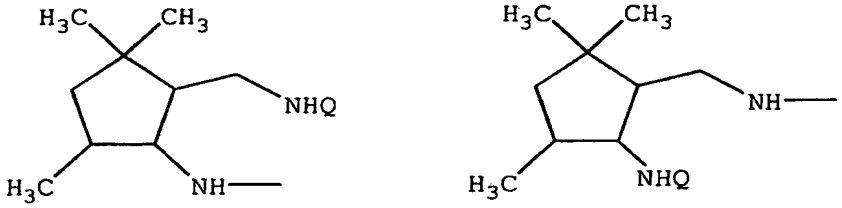
Formula (I)

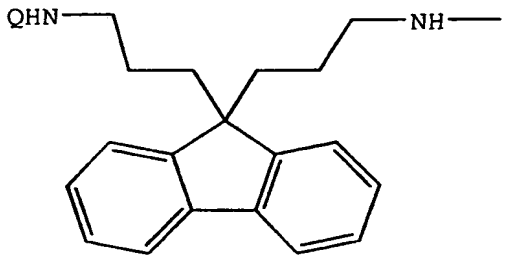
wherein:

T, U and V are independently selected from an oxygen, sulfur or nitrogen atom, provided that at least two of T, U and V are a nitrogen atom;

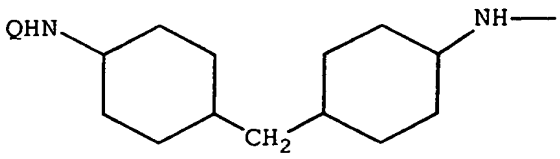
X_1 is selected from the group consisting of H, $-NHC(O)NR_1R_2$, $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$, and $-CH_2NR_1R_2$, wherein R_1 is a hydrogen atom or a functionalized resin, and R_2 is a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, the formulae:







and



wherein Q is a hydrogen atom or functionalized resin;

X_2 is selected from the group consisting of C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_2 to C_7 alkenylene, C_2 to C_7 substituted alkenylene, C_2 to C_7 alkynylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, C_5 to C_7 cycloalkenylene, C_5 to C_7 substituted cycloalkenylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, C_7 to C_{12} substituted phenylalkylene, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy,

the formula:

$$-(CH_2)_m-G-(CH_2)_n-$$

wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and G is selected from phenylene and substituted phenylene,

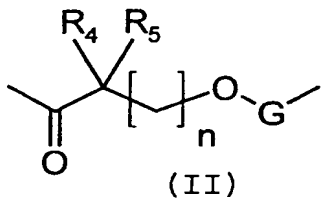
the formula:

$$-(CH_2)_m-NR_3-(CH_2)_n-$$

wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and R_3 is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_4 alkyl sulfonyl, C_1 to C_4 substituted alkyl sulfonyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl,

substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl, substituted phenylaminothiocarbonyl, C_1 to C_7 alkoxycarbonyl, C_1 to C_7 substituted alkoxycarbonyl, phenoxycarbonyl and substituted phenoxycarbonyl,

the formula:

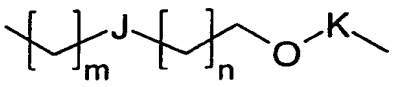


(II)

wherein n is an integer selected from 0 to 6; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl and protected

hydroxymethyl; and G is selected from phenylene and substituted phenylene, and

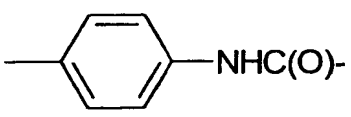
the formula:



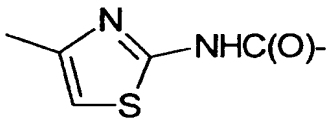
(III)

wherein J and K are each selected from the group consisting of phenylene and substituted phenylene, and m and n are independently selected from 0 and 1, and

the formulae (IV) and (V):

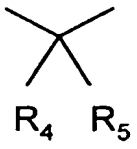


(IV)



(V) ; and

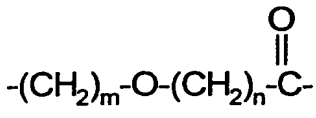
X_3 is absent or is selected from the group consisting of the formula:



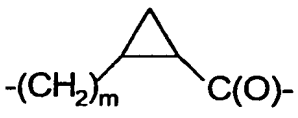
wherein:

R_4 and R_5 are together or independently selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_1 to C_6 substituted alkyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl and protected hydroxymethyl,

the formulae (VIa) and (Vib):



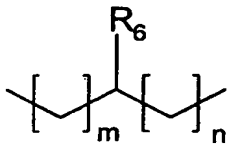
(VIa)



(VIb)

wherein in formula (VIa) m and n are independently selected from 0, 1, 2, 3 and 4; and wherein in formula (VIb) m is selected from 0, 1, 2, 3 and 4;

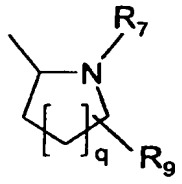
the formula:



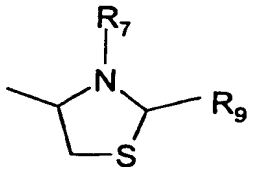
wherein R_6 is selected from the group consisitng of a hydrogen atom, amino, amino-protecting group, $-NR_7R_8$, carboxy, carboxy-protecting group, $-C(O)NR_7R_8$, wherein R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted

phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and m and n are independently selected from 0, 1, 2, 3 and 4; and

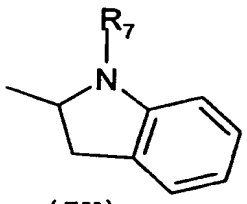
the formulae (VII) to (XIII):



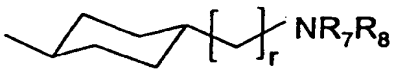
(VII)



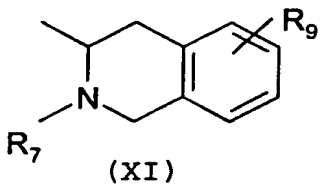
(VIII)



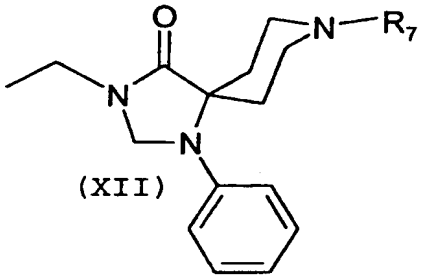
(IX)



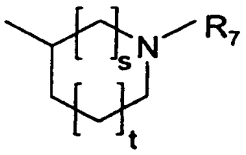
(X)



(XI)



(XII)

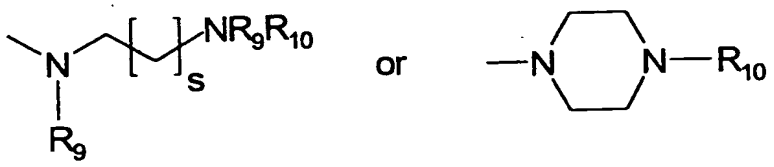


(XIII)

wherein q is 1 or 2; r is 0 or 1; s and t are independently selected from 0, 1 or 2; and R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and R_9 is selected from a hydrogen atom, -OH, hydroxy-protecting group, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 phenylalkoxy, phenyl, substituted phenyl, heteroaryl and substituted heteroaryl; and

X_4 is absent or is selected from the group consisting of a hydrogen atom, -OH, $-CO_2H$, $-C(O)NR_7R_8$ and $-NR_7R_8$, wherein R_7 and R_8 are independently selected from a functionalized resin, a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl,

and the formulae:



wherein R_9 and R_{10} are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and s is an integer selected from 1 to 5;

a pharmaceutically acceptable salt of a compound thereof; or

a biologically active ester form of a compound thereof.

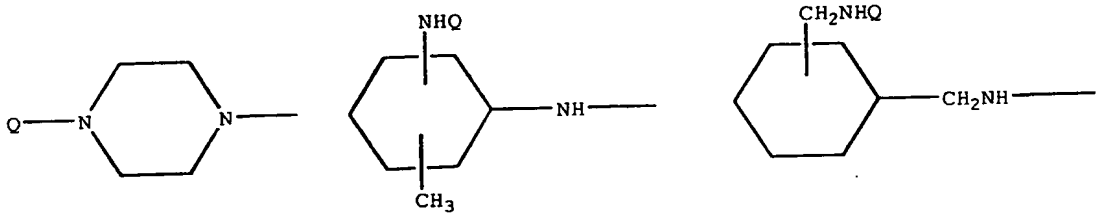
8. The combinatorial library of claim 7, wherein one of T, U and V is oxygen and the other two positions are each nitrogen.

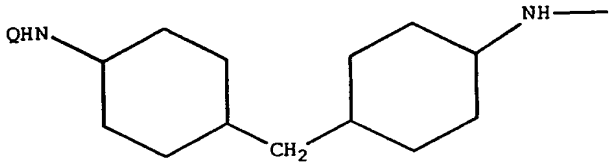
9. The combinatorial library of claim 8, wherein U is oxygen, T is nitrogen and V is nitrogen.

10. The combinatorial library of claim 7, wherein

X_1 is selected from the group consisitng of $-CO_2R_1$, $-OR_1$, NR_1R_2, $-C(O)NR_1R_2$,

and the formulae:



and 

;

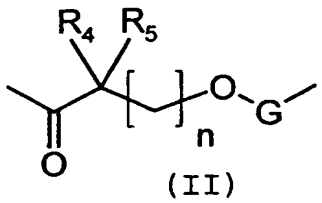
X_2 is selected from the group consisting of C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, C_7 to C_{12} substituted phenylalkylene,

the formula:

$$-(CH_2)_m-NR_3-(CH_2)_n-$$

wherein m is 1 to 3 and n is 1 to 4,

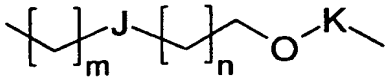
and the formula:



(II)

wherein n is 0 or 1; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl or C_1 to C_{10} substituted alkyl,

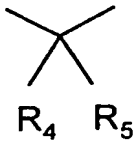
and the formula:



(III)

wherein m and n are integers independently selected from 0 and 1;

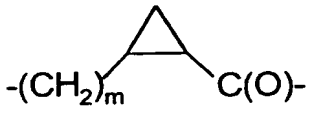
X_3 is absent or the formula:



wherein:

R_4 and R_5 are together or independently selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_7 to C_{12} substituted phenylalkyl, substituted phenyl, hydroxymethyl, protected hydroxymethyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl,

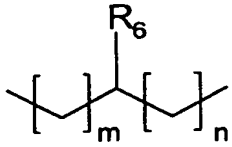
the formula:



(VIb)

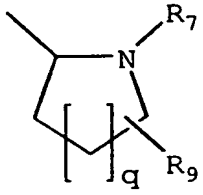
wherein m is 0,

and the formula:



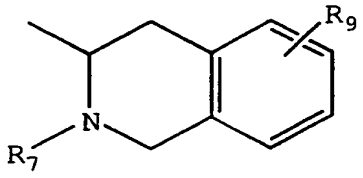
wherein m is 0 to 2 and n is 1 to 4; and

where X_3 is absent, X_4 is selected from the group consisting of the formulae:

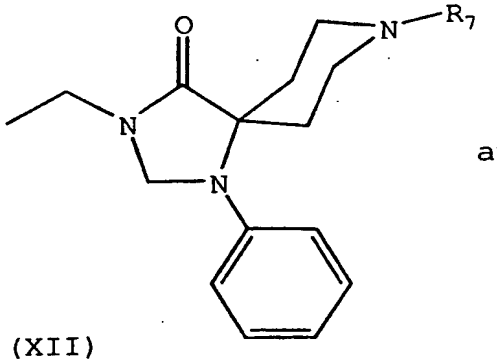


(VII)

(X)

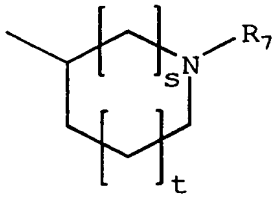


(XI)



(XII)

and



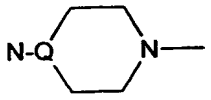
(XIII)

wherein R_9 is selected from a hydrogen atom and -OH.

11. The combinatorial library of claim 7, wherein:

X_1 is selected from the group consisting of $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$,

and the formula:



12. The combinatorial library of claim 9, wherein:

X_1 is selected from the group consisting of OH, $CONH_2$, 2-(1-pyrrolidino)ethylamine, 2-pyridinemethylamine, 2-(4-imidazole)ethylamine, cyclopentylamine, allylamine, 2-methoxyethylamine, (+/-)-tetrahydrofurylamine, benzylamine, 2-methylbenzylamine, 3-methylbenzylamine, 4-methylbenzylamine, 2-fluorobenzylamine, 3-fluorobenzylamine, 4-fluorobenzylamine, 3-(1-imidazole)propylamine, 4-aminomethylbenzylamine, 4-methoxybenzylamine, 3-chlorobenzylamine, 3-bromobenzylamine, 4-bromobenzylamine, cyclopropylamine, cyclopropanemethylamine, 4-pyridinemethylamine, 3-pyridinemethylamine, 2-thiophenemethylamine, phenethylamine, 2-(morpholine)ethylamine, 3-methoxybenzylamine, piperonylamine, 4-methoxyphenethylamine, 2-fluorophenethylamine, 2-(4-chlorophenyl)ethylamine, 2-(3-chlorophenyl)ethylamine, 2-(2-chlorophenyl)ethylamine, 2,3-dimethoxybenzylamine, 3,4-dimethoxyphenethylamine, 2,4-dichlorophenethylamine, 2-(diethylamino)ethylamine, 2-(1-methylpyrrolidin-2-yl)ethylamine, 3-(diethylamino)propylamine, 2-(5-nitro-2-pyridyl)ethylamine, 3-(dimethylamino)-2,2-dimethylpropylamine, 3-(dimethylamino)propylamine, 2-aminoethylamine, 2-(piperidino)ethylamine, isoamylamine,

3-ethoxypropylamine, 3-(2-pipecolinyl)propylamine, 3-butoxypropylamine, 3-(pyrrolidin-2-one-1-yl)propylamine, 3-(morpholino)propylamine, 2-(N-ethyl-3-methylanilino)ethylamine, 3-phenyl-1-propylamine, 2-methyl-2-phenylethylamine, 4-phenylbutylamine, 3,3-diphenylpropylamine, isobutylamine, 2-(2-pyridyl)ethylamine, cyclohexanemethylamine, 3-methoxyphenethylamine, 3-phenylbenzylamine, and piperazine;

X_2 is selected from the group consisting of methylene, 1,1-cyclopropyl, 1,3-phenylene, 1,4-phenylene, 1-methyl-1-(4-oxyphenylene)ethane, 3-methoxy-1,4-phenylene, 2-fluoro-1,4-phenylene, 4,4'-biphenylene, 1,2-phenylene, 3,5-dibromo-1,4-phenylene, 4-phenyl-1-(methylene-1-yl), 3,5-diiodo-1,4-phenylene, 3-hydroxy-1,4-phenylene, 2,3,5,6-tetrafluoro-1,4-phenylene, 3-bromo-1,4-phenylene, 3,5-di-tert-butyl-1,4-phenylene, 3,5-di-tert-butyl-4-phenyl-1-(methylene-1-yl), 3-methoxy-4-phenyl-1-(methylene-1-yl), 3-nitro-1,4-phenylene, 5-hydroxy-1,3-phenylene, 4-phenyl-1-(-2-ethyl), 3-ethoxy-4-phenyl-1-(methylene-1-yl), 2-chloro-1,4-phenylene, 2-fluoro-1,4-phenylene, 3,5-dimethyl-1,4-phenylene, 2,6-dimethyl-1,4-phenylene, 3,5-dichloro-1,4-phenylene, 3-methoxy-2-phenyl-1-(methylene-1-yl), 8-quinoline-2-yl, 5-indole-3-(methylene-1-yl), 3,hydroxy-4-phenyl-1-(methylene-1-yl), 4-chloro-1,2-phenylene, 6-nitro-1,2-phenylene, 5-nitro-1,2-phenylene, 2-amino-1,4-phenylene,2-carboxymethyl-1,4-phenylene,

3-bromo-5-methoxy-4-phenyl-1-(methylene-1-yl),
3,5-dimethoxy-4-phenyl-1-(methylene-1-yl),
2-iodo-6-nitro-1,4-phenylene;

X_3 is selected from the group consisting of
1-aminomethylene,
1-(1-aminoethyl),1-(2-aminoethyl),
1-(1-amino-2-(3-pyridyl)ethyl),
1-(1-amino-2-(2-thienyl)ethyl), 1-(1-aminopropyl),
1-(3-aminopropyl), 1-(5-aminopentyl),
1-(1-methyl-1-aminoethyl),
1-(4-aminomethylcyclohexyl),
1-(1-amino-3-guanidinopropyl), 3-(3-aminopropionic acid), 3-(2-aminopropionic acid),
3-methylene-1-phenyl-1,3,8-triazaspiro[4.5]decane-4-one, 1-(1-amino-2-(4-chlorophenyl)ethyl),
1-(1-amino-2-(cyclohexyl)ethyl), 4-(4-aminobutyric acid), 4-(2-aminobutyric acid),
1-(1-amino-2-(4-imidazolyl)ethyl),
1-(1-amino-2-methylbutyl), 4-piperidinyl,
1-(1-amino-3-methylbutyl), 3-piperidinyl,
1-(1-aminobutyl), 1-(1-amino-2-phenylethyl),
2-piperidinyl, 2-pyrrolidinyl,
1-(1-amino-2-hydroxyethyl), 4-thiazolidinyl,
1-(1-amino-2-hydroxypropyl),
3-tetrahydroisoquinolinyl,
1-(1-amino-2-(3-indolyl)ethyl),
1-(1-amino-2-(4-hydroxyphenyl)ethyl),
1-(1-amino-2-(4-ethoxyphenyl)ethyl), 1-(1-amino-2-methylpropyl), 1-(1,5-diaminopentyl),
2-(1-pyrrolidino)ethylaminomethylene,
2-pyridinemethylaminomethylene,
2-(4-imidazole)ethylaminomethylene,
cyclopentylaminomethylene, allylaminomethylene,
2-methoxyethylaminomethylene,
(+/-)-tetrahydrofurylaminomethylene,
benzylaminomethylene, 2-methylbenzylaminomethylene,

3-methylbenzylaminomethylene,
4-methylbenzylaminomethylene,
2-fluorobenzylaminomethylene,
3-fluorobenzylaminomethylene,
4-fluorobenzylaminomethylene,
3-(1-imidazole)propylaminomethylene,
4-aminomethylbenzylaminomethylene,
4-methoxybenzylaminomethylene,
3-chlorobenzylaminomethylene,
3-bromobenzylaminomethylene,
4-bromobenzylaminomethylene,
cyclopropylaminomethylene,
cyclopropanemethylaminomethylene,
4-pyridinemethylaminomethylene,
3-pyridinemethylaminomethylene,
2-thiophenemethylaminomethylene,
phenethylaminomethylene,
2-(morpholine)ethylaminomethylene, 3-methoxybenzylaminomethylene,
piperonylaminomethylene,
4-methoxyphenethylaminomethylene,
2-fluorophenethylaminomethylene,
2-(4-chlorophenyl)ethylaminomethylene,
2-(3-chlorophenyl)ethylaminomethylene,
2-(2-chlorophenyl)ethylaminomethylene,
2,3-dimethoxy- benzylaminomethylene,
3,4-dimethoxyphenethylaminomethylene, 2,4-dichlorophenethylaminomethylene,
2-(diethylamino)ethylaminomethylene,
2-(1-methylpyrrolidin-2-yl)ethylaminomethylene,
3-(diethylamino)propylaminomethylene,
2-(5-nitro-2-pyridyl)ethylaminomethylene,
3-(dimethylamino)-2,2-dimethylpropylaminomethylene,
3-(dimethylamino)propylaminomethylene,
2-aminoethylaminomethylene,
2-(piperidino)ethylaminomethylene,
isoamylaminomethylene, 3-ethoxypropylaminomethylene,

3-(2-pipecolinyl)propylaminomethylene,
3-butoxypropylaminomethylene,
3-(pyrrolidin-2-one-1-yl)propylaminomethylene,
3-(morpholino)propylaminomethylene,
2-(N-ethyl-3-methylanilino)ethylaminomethylene,
3-phenyl-1- propylaminomethylene,
2-methyl-2-phenylethylaminomethylene,
4-phenylbutylaminomethylene,
3,3-diphenylpropylaminomethylene,
isobutylaminomethylene,
2-(2-pyridyl)ethylaminomethylene,
cyclohexanemethylaminomethylene,
3-methoxyphenethylaminomethylene,
3-phenylbenzylaminomethylene, and
piperazinomethylene; and

X_4 is selected from the group consisting of acetyl, alpha-methylcinnamyl, benzoyl, crotonyl, cyclobutanecarbonyl, cyclohexanepropionyl, 4-cyanobenzoyl, hydrocinnamyl, 4-dimethylaminobenzoyl, 4-ethoxybenzoyl, isobutyryl, 4- ethoxyphenylacetyl, isovaleryl, levulinyl, m-anisyl, m-toluyl, methoxyacetyl, isonicotinyl, p-tolylacetyl, picolinyl, piperonylyl, 4-fluoro-alpha- methylphenylacetyl, 4-fluorophenylacetyl, tetrahydro-3-furoyl, trans-3-(3-pyridyl)acrylyl, trimethylacetyl, triphenylacetyl, nicotinyl, (3,4-dimethoxyphenyl)acetyl, boc-isonipecotyl, (alpha-alpha-alpha-trifluoro-m-tolyl)acetyl, (methylthio)acetyl, (phenylthio)acetyl, 1-(4-chlorophenyl)-1- cyclopentanecarbonyl, 1-adamantaneacetyl, 1-naphthylacetyl, 1-phenyl-1-cyclopropanecarbonyl, 4-iodobenzoyl, 4-isopropoxybenzoyl, 2,4-dichlorobenzoyl, 4-methyl-1-cyclohexanecarbonyl, pyrrole-2- carbonyl, 4-methylvaleryl, 1- naphthylacetyl, 2-fluorobenzoyl,

1,3-phenylene diacetyl, 2-norbornaneacetyl, 2-pyrazinecarbonyl, 2-pyridylacetyl, 2-thiopheneacetyl, 3,4,5- triethoxybenzoyl, 3,4-methylenedioxyphenylacetyl, 3,4-dichlorobenzoyl, 4- isopropylbenzoyl, 3,4-dichlorophenylacetyl, 4-tert-butyl-cyclohexanecarbonyl, 4-sulfonamidobenzoyl, 3,5,5-trimethylhexanoyl, 3,5-bis(trifluoromethyl)-benzoyl, 5-bromo-2-chlorobenzoyl, 5-bromonicotinyl, 6-chloronicotinyl, 3,5-dimethyl-p-anisyl, 3-bromo-4-methylbenzoyl, 3,4,5-trimethoxyphenylacetyl, 3-benzoylpropionyl, 3,5-dichlorobenzoyl, 3-cyanobenzoyl, 3-fluoro-4-methylbenzoyl, 1-isoquinolinecarbonyl, 3-methyl-2-thiophenecarbonyl, 3-phenoxybenzoyl, 3-thiopheneacetyl, 4- biphenylacetyl, 4-bromophenylacetyl, s-(+)-mandelyl, 3,5-di-tert-butyl-4-hydroxybenzoyl, 3,5-dichloro-4-hydroxybenzoyl, 4- hydroxybenzoyl, 5-methylsalicylyl, 2- methylcyclopropanecarbonyl, 3-lndolepropionyl, 2,2-diphenylacetyl, 5-methoxyindole-2-carbonyl, succinamyl, 4-dimethylaminobutyryl, 4- methylthiobenzoyl, 2-methylthionicotinyl, r(-)-2-oxothiazolidine-4-carbonyl, 4-nitrophenylacetyl, coumarin-3-carbonyl, 1-cyano-1-cyclopropane carbonyl, 2-chloro-5-(methylthio)benzoyl, theophylline-7-acetyl, 2-(2-cyanophenylthio)benzoyl, 2-mesitylenesulfonyl, 2-naphthalenesulfonyl, 2-thiophenesulfonyl, 4-chlorobenzenesulfonyl, 4-fluorobenzenesulfonyl, 4-methoxybenzenesulfonyl, 4-methylsulfonylbenzenesulfonyl, benzenesulfonyl, dansyl, n-acetylsulfanilyl, 2-acetamido-4-methyl-5-thiazolesulfonyl, 4-(trifluoromethoxy)benzenesulfonyl, 4-tert-butylbenzenesulfonyl, 8-quinolinesulfonyl,

2,3-dichlorothiophene-5-sulfonyl, 3,4-dimethoxybenzenesulfonyl, 3,5-bis(trifluoromethyl)benzenesulfonyl, 3-chloro-4-fluorobenzenesulfonyl, 3-trifluoromethylbenzenesulfonyl, 4-ethylbenzenesulfonyl, pentamethylbenzenesulfonyl, 2,3,4-trifluorobenzenesulfonyl, 2,4-dichlorobenzenesulfonyl, 2,5-dichlorothiophene-3-sulfonyl, 2,6-dichlorobenzenesulfonyl, 2,6-difluorobenzenesulfonyl, 2-chloro-4-(trifluoromethyl)benzenesulfonyl, 2-chloro-5-(trifluoromethyl)benzenesulfonyl, 2-chloro-6-methylbenzenesulfonyl, 3,4-difluorobenzenesulphonyl, 3,5-dichlorobenzenesulfonyl, 3-chlorobenzenesulfonyl, 4-(n- butoxy)benzenesulfonyl, 4-trifluoromethylbenzene sulfonyl, 3,5-dimethylisoxazole-4-sulfonyl, 2-(methoxycarbonyl)thiophene-3-sulfonyl, 4-acetamido-3-chlorobenzene sulfonyl, 2-[1-methyl-5-(trifluoromethyl)pyrazol-3-yl]thiophene-5-sulfonyl, 2-(benzoylaminomethyl)thiophene-5-sulfonyl, 3-methoxy-4-(methoxycarbonyl)-thiophene-2-sulfonyl, 5-(isoxazol-3- yl)thiophene-2-sulfonyl, 4-cyanobenzene sulfonyl, 3-chloro-4-methylbenzenesulfonyl, 2,4-difluorobenzenesulfonyl, 2-fluorobenzenesulfonyl, 4-isopropylbenzene sulfonyl, 2,5-dimethoxybenzenesulfonyl, 3,4-dichlorobenzenesulfonyl, (2s,3s)-2-(carbamyl)-3-methylvalerate methyl ester, (r)-(-)-1-(carbamyl)-(1-naphthyl)ethane, (s)-(+)-1-(carbamyl)-(1-naphthyl)ethane, (s)-(+)-2-(carbamyl)-3-tert-butoxypropionate methyl ester, (s)-(-)-2-(carbamyl)-3-methylbutyrate methyl

ester, (s)-(-)-2-(carbamyl)-4-(methylthio)butyrate methyl ester, (s)-(-)-2-(carbamyl)-4-methylvalerate methyl ester, (s)-(-)-2-(carbamyl)glutarate diethyl ester, (s)-(-)-2-(carbamyl)propionate methyl ester, (s)-2-(carbamyl)-3- phenylpropionate methyl ester, 1-(carbamyl)-tridecafluoro-1-hexane, 1-(carbamyl)-1,1,3,3-tetramethylbutane, 1-(carbamyl)-(1-naphthyl)ethane, 1-(carbamyl)-(4-bromophenyl)ethane, 1-(carbamyl)-adamantane, 1-(carbamyl)naphthalene, 1-(carbamyl)-2,3,4-trifluorobenzene, 1-(carbamyl)-2,3-dichlorobenzene, 1-(carbamyl)-2,3-dimethylbenzene, 1-(carbamyl)-2,4,5-trichlorobenzene, 1-(carbamyl)-2,4,5-trimethylbenzene, 1-(carbamyl)-2,4,6-trichlorobenzene, 1-(carbamyl)-2,4-dichlorobenzene, 1-(carbamyl)-2,4-difluorobenzene, 1-(carbamyl)-2,4-dimethoxybenzene, 1-(carbamyl)-2,4-dimethylbenzene, 1-(carbamyl)-2,5-dichlorobenzene, 1-(carbamyl)-2,5-difluorobenzene, 1-(carbamyl)-2,5-dimethoxybenzene, 1-(carbamyl)-2,5-dimethylbenzene, 1-(carbamyl)-2,6-dibromo-4-fluorobenzene, 1-(carbamyl)-2,6-dibromo-4-isopropylbenzene, 1-(carbamyl)-2,6-dichlorobenzene, 1-(carbamyl)-2,6-diethylbenzene, 1-(carbamyl)-2,6-difluorobenzoyl, 1-(carbamyl)-2,6-difluorobenzene,1-(carbamyl)-2,6-di isopropylbenzene, 1-(carbamyl)-2,6-dimethylbenzene, 1-(carbamyl)-2-(chloromethyl)benzene, 1-(carbamyl)-2-(difluoromethoxy)benzene, 1-(carbamyl)-2-(methylthio)benzene, 1-(carbamyl)-2-(trifluoromethoxy)benzene, 1-(carbamyl)-2-(trifluoromethyl)benzene, 1-(carbamyl)-2-biphenyl, 1-(carbamyl)-2-bromo-4,6-difluorobenzene,

1-(carbamyl)-2-bromoethane,
1-(carbamyl)-2-bromobenzene,
1-(carbamyl)-2-chloro-4-nitrobenzene,
1-(carbamyl)-2-chloro-5-(trifluoromethyl)benzene,
1-(carbamyl)-2-chloro-5- nitrobenzene,
1-(carbamyl)-2-chloro-6-methylbenzene,
1-(carbamyl)-2-chlorobenzyl,
1-(carbamyl)-2-chloroethane,
1-(carbamyl)-2-chlorobenzene,
1-(carbamyl)-2-cyanobenzene,
1-(carbamyl)-2-ethoxybenzene,
1-(carbamyl)-2-ethyl-6-methylbenzene,
1-(carbamyl)-2-ethylbenzene,
1-(carbamyl)-2-fluoro-3-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluoro-5-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluoro-5-methylbenzene,
1-(carbamyl)-2-fluoro-5-nitrobenzene,
1-(carbamyl)-2-fluoro-6-(trifluoromethyl)benzene,
1-(carbamyl)-2-fluorobenzene,
1-(carbamyl)-2-iodobenzene,
1-(carbamyl)-2-isopropyl-6-methylbenzene,
1-(carbamyl)-2-isopropylbenzene,
1-(carbamyl)-2-methoxy-5-chloro benzene,
1-(carbamyl)-2-methoxy-5-methylbenzene,
1-(carbamyl)-2-methoxy-5-nitrobenzene,
1-(carbamyl)-2-methoxybenzene,
1-(carbamyl)-2-methyl-3-nitrobenzene,
1-(carbamyl)-2-methyl-5-nitrobenzene,
1-(carbamyl)-2-methyl-6-t-butylbenzene,
1-(carbamyl)-1-(2-methylphenyl)methane,
1-(carbamyl)-2-n-propylbenzene,
1-(carbamyl)-2-naphthalene,
1-(carbamyl)-2-nitrobenzene,
1-(carbamyl)-2-phenoxybenzene,
1-(carbamyl)-2-tert-butylbenzene,
1-(carbamyl)-3,4,5-trimethoxybenzene,
1-(carbamyl)-1-(3,4-dichlorophenyl)methane,

1-(carbamyl)-3,4-dichlorobenzene,
1-(carbamyl)-3,4-difluorobenzene,
1-(carbamyl)-3,4-dimethylbenzene,
1-(carbamyl)-3,5-bis(trifluoromethyl)benzene,
1-(carbamyl)-3,5- dichlorobenzene,
1-(carbamyl)-3,5-dimethoxybenzene,
1-(carbamyl)-3,5-dimethylbenzene, 1-(carbamyl)-3,5-dinitrobenzene, 1-(carbamyl)-3-(methylthio)benzene,
1-(carbamyl)-3-(trifluoromethyl)benzene,
1-(carbamyl)-3-(trifluoromethylthio)benzene,
1-(carbamyl)-3-acetylbenzene,
1-(carbamyl)-3-bromobenzene,
1-(carbamyl)-3-bromopropane,
1-(carbamyl)-3-carbomethoxybenzene,
1-(carbamyl)-3-chloro-2-methoxybenzene,
1-(carbamyl)-3-chloro-2-methylbenzene,
1-(carbamyl)-3-chloro-4-fluorobenzene,
1-(carbamyl)-3-chloro-4-methylbenzene,
1-(carbamyl)-3-chlorobenzene,
1-(carbamyl)-3-chloropropane,
1-(carbamyl)-3-cyanobenzene,
1-(carbamyl)-3-cyclopentoxy-4-methoxybenzene,
1-(carbamyl)-3-ethylbenzene,
1-(carbamyl)-3-fluoro-4-methylbenzene,
1-(carbamyl)-3-fluorobenzene,
1-(carbamyl)-3-iodopropane, 3-(carbamyl)benzoyl chloride, 1-(carbamyl)-3-methoxybenzene,
1-(carbamyl)-(3-methylphenyl)methane,
1-(carbamyl)-3-nitrobenzene,
1-(carbamyl)-3-pyridine,
4'-(carbamyl)-5'-nitrobenzo-15-crown-5,
4'-(carbamyl)benzo-15-crown-5,
4'-(carbamyl)benzo-18-crown-6,
1-(carbamyl)-4,5-dimethyl-2-nitrobenzene,
1-(carbamyl)-4-(6-methyl-2-benzothiazolyl)benzene,
1-(carbamyl)-4-(chloromethyl)benzene,
1-(carbamyl)-4-(chlorosulfonyl)benzene,

1-(carbamyl)-4-(difluoromethoxy)benzene,
1-(carbamyl)-4-(methylthio)benzene,
1-(carbamyl)-4-(tert-butyl)benzene,
1-(carbamyl)-4-(trifluoromethoxy)benzene,
1-(carbamyl)-4-(trifluoromethyl)benzene,
1-(carbamyl)-4-(trifluoromethylthio)benzene,
1-(carbamyl)-4-acetylbenzene,
1-(carbamyl)-4-benzyloxybenzene,
1-(carbamyl)-4-bromo-2,6-dimethylbenzene,
1-(carbamyl)-4-bromo-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-bromo-2-chlorobenzene,
1-(carbamyl)-4-bromo-2-fluorobenzene,
1-(carbamyl)-4-bromo-2-methylbenzene,
1-(carbamyl)-4-bromobenzene,
1-(carbamyl)-4-chloro-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-chloro-2-methoxybenzene,
1-(carbamyl)-4-chloro-2-methylbenzene,
1-(carbamyl)-4-chloro-2-nitrobenzene,
1-(carbamyl)-4-chloro-3-(trifluoromethyl)benzene,
1-(carbamyl)-4-chloro-3-nitrobenzene,
1-(carbamyl)-4-chlorobenzene,
1-(carbamyl)-4-dimethylaminobenzene,
1-(carbamyl)-4-ethoxybenzene,
1-(carbamyl)-4-ethylbenzene,
1-(carbamyl)-4-fluoro-2-(trifluoromethyl)benzene,
1-(carbamyl)-4-fluoro-2-nitrobenzene,
1-(carbamyl)-4-fluoro-3-(trifluoromethyl)benzene,
1-(carbamyl)-4-fluoro-3-nitrobenzene,
1-(carbamyl)-4-fluorobenzoyl,
1-(carbamyl)-4-fluorobenzyl,
1-(carbamyl)-4-fluorobenzene,
1-(carbamyl)-4-heptyloxybenzene,
1-(carbamyl)-4-iodobenzene, 4-(carbamyl)benzoyl chloride, 1-(carbamyl)-4-isopropylbenzene,
1-(carbamyl)-4-methoxy-2-methylbenzene,
1-(carbamyl)-(4-methoxyphenyl)methane,
1-(carbamyl)-4-methoxybenzene,

1-(carbamyl)-4-methyl-2-nitrobenzene,
1-(carbamyl)-4-methyl-3-nitrobenzene,
1-(carbamyl)-(4-methylphenyl)methane,
1-(carbamyl)-4-n-butoxycarbonylbenzene,
1-(carbamyl)-4-n-butoxybenzene,
1-(carbamyl)-4-n-butyl-2-methylbenzene,
1-(carbamyl)-4-n-butylbenzene,
1-(carbamyl)-4-nitrobenzene,
1-(carbamyl)-4-phenoxybenzene,
1-(carbamyl)-5-bromopenane,
1-(carbamyl)-5-chloro-2,4-dimethoxybenzene,
1-(carbamyl)-5-chloro-2-methylbenzene,
1-(carbamyl)-5-fluoro-2-methylbenzene,
1-(carbamyl)-5-iodopentane, 1-(carbamyl)-2-propene,
benzoyl carbamyl, 1-(carbamyl)-1-phenylmethane,
1-(carbamyl)-cyclohexane, carboxyethylcarbamyl,
ethyl 2-(carbamyl)-3-methylbutyrate, ethyl
2-(carbamyl)-3-phenylpropionate, ethyl
2-(carbamyl)-4- (methylthio)butyrate, ethyl
2-(carbamyl)-4-methylvalerate, ethyl
2-(carbamyl)benzoate, ethyl 2-(carbamyl)propionate,
ethyl 3-(carbamyl)benzoate, ethyl
3-(carbamyl)propionate, ethyl 4-(carbamyl)-benzoate,
ethyl 6-(carbamyl)hexanoate, 1-(carbamyl)-ethyl,
ethyl(carbamyl)acetate, 1-(carbamyl)-heptane,
1-(carbamyl)-hexane, 1-(carbamyl)-2-methylpropane,
1-(carbamyl)ethyl methacrylate,
1-(carbamyl)-2-methylethane, methyl
2-(carbamyl)benzoate, carbamylmethane,
methyl(carbamyl)propionate, 1-(carbamyl)butane,
n-butyl (carbamyl)acetate, 1-(carbamyl)-propane,
1-(carbamyl)-pentane, 1-(carbamyl)-phenylthane,
1-(carbamyl)-benzene,
1-(carbamyl)-2,2-dimethylpropane,
1-(carbamyl)-tetrahydro-2-pyran,
1-(carbamyl)-trans-2-benzenecyclopropane,
1-(carbamyl)-trichloroacetate,

carbamyltrichloromethane,
1-(thiocarbamyl)-(2-methoxy-5-phenyl)benzene,
1-(thiocarbamyl)adamantane,
1-(thiocarbamyl)naphthalenemethane,
(thiocarbamyl)naphthalene,
1-(thiocarbamyl)2,2-diphenylethane,
1-(thiocarbamyl)-2,3,4,5-tetrachlorobenzene,
1-(thiocarbamyl)-2,3,4-trichlorobenzene,
1-(thiocarbamyl)-(2,3,4-trimethoxyphenyl)methane,
1-(thiocarbamyl)-2,3,5,6-tetrachlorobenzene,
1-(thiocarbamyl)-2,3,5,6-tetrafluorobenzene,
1-(thiocarbamyl)-2,3-dibromopropane,
1-(thiocarbamyl)-2,3-dichlorobenzene,
1-(thiocarbamyl)-(2,3-dimethoxyphenyl)methane,
1-(thiocarbamyl)-2,3-dimethylbenzene,
1-(thiocarbamyl)-2,4,5-trichlorobenzene,
1-(thiocarbamyl)-2,4,6-tribromobenzene,
1-(thiocarbamyl)-2,4,6-trichlorobenzene,
1-(thiocarbamyl)-2,4,6-trifluorobenzene,
1-(thiocarbamyl)-2,4,6-trimethylbenzene,
1-(thiocarbamyl)-2,4-dichlorobenzene,
1-(thiocarbamyl)-2,4-difluorobenzene,
1-(thiocarbamyl)-2,4-dimethoxybenzene,
1-(thiocarbamyl)-2,4-dimethylbenzene,
1-(thiocarbamyl)-2,5-dibromobenzene,
1-(thiocarbamyl)-2,5-dichlorobenzene,
1-(thiocarbamyl)-2,5-difluorobenzene,
1-(thiocarbamyl)-2,5-dimethoxybenzene,
1-(thiocarbamyl)-2,5-dimethylbenzene,
1-(thiocarbamyl)-2,6-dichlorobenzene,
1-(thiocarbamyl)-2,6-diethylbenzene,
1-(thiocarbamyl)-2,6-difluorobenzene,
1-(thiocarbamyl)-2,6-diisopropylbenzene,
1-(thiocarbamyl)-2,6-dimethylbenzene,
1-(thiocarbamyl)-2-(3,4-dimethoxyphenyl)ethane,
1-(thiocarbamyl)-2-(4-chlorophenyl)ethane,
1-(thiocarbamyl)-2-(methylthio)benzene,

1-(thiocarbamyl)-2-(trifluoromethoxy)benzene,
1-(thiocarbamyl)-2-(trifluoromethyl)benzene,
1-(thiocarbamyl)-2-bromo-4-methylbenzene,
1-(thiocarbamyl)-2-bromoethane,
1-(thiocarbamyl)-2-bromobenzene,
1-(thiocarbamyl)-2-chloro-4-methylbenzene,
1-(thiocarbamyl)-2-chloro-4-nitrobenzene,
1-(thiocarbamyl)-2-chloro-5-(trifluoromethyl)benzene
, 1-(thiocarbamyl)-2-chloro-5-nitrobenzene,
1-(thiocarbamyl)-2-chloro-6-methylbenzene,
1-(thiocarbamyl)-(2-chlorophenyl)methane,
1-(thiocarbamyl)-2-chloroethane,
1-(thiocarbamyl)-2-chlorobenzene,
1-(thiocarbamyl)-2-cyanobenzene,
1-(thiocarbamyl)-2-ethoxycarbonylbenzene,
1-(thiocarbamyl)-2-ethoxybenzene,
1-(thiocarbamyl)-2-ethyl-6-(1-methylpropyl)benzene,
1-(thiocarbamyl)-2-ethyl-6-isopropylbenzene,
1-(thiocarbamyl)-2-ethyl-6-methylbenzene,
1-(thiocarbamyl)-2-ethylbenzene,
1-(thiocarbamyl)-(2-fluorophenyl)methane,
1-(thiocarbamyl)-2-fluoroethane,
1-(thiocarbamyl)-2-fluorobenzene,
2-(thiocarbamyl)furan, 2-(thiocarbamyl)hexane,
1-(thiocarbamyl)-2-iodobenzene,
1-(thiocarbamyl)-2-isopropyl-6-methylbenzene,
1-(thiocarbamyl)-2-isopropylbenzene,
1-(thiocarbamyl)-2-methoxy-4-nitrobenzene,
1-(thiocarbamyl)-2-methoxy-5-methylbenzene,
1-(thiocarbamyl)-2-methoxy-5-nitrobenzene,
1-(thiocarbamyl)-(2-methoxyphenyl)methane,
1-(thiocarbamyl)-2-methoxyethane,
1-(thiocarbamyl)-2-methoxybenzene,
1-(thiocarbamyl)-2-methyl-4-nitrobenzene,
1-(thiocarbamyl)-2-methyl-5-nitrobenzene,
1-(thiocarbamyl)-(2-methylphenyl)methane,
1-(thiocarbamyl)-2-methylbutane,

1-(thiocarbamyl)-2-(morpholino)ethane,
2-(thiocarbamyl)-naphthalene,
2-(thiocarbamyl)pentane,
1-(thiocarbamyl)-2-phenylethane,
1-(thiocarbamyl)-2-piperidinoethane,
2-(thiocarbamylmethyl)-tetrahydrofuran,
1-(thiocarbamyl)-3,4,5-trimethoxybenzene,
1-(thiocarbamyl)-3,4-(ethylenedioxy)benzene,
1-(thiocarbamyl)-3,4-dichlorophenyl)methane,
1-(thiocarbamyl)-3,4-dichlorobenzene,
1-(thiocarbamyl)-(3,4-dimethoxyphenyl)methane,
1-(thiocarbamyl)-3,4-dimethoxybenzene,
1-(thiocarbamyl)-3,4-dimethylbenzene,
1-(thiocarbamyl)-(3,4-methylenedioxyphenyl)methane,
1-(thiocarbamyl)-3,4-methylenedioxybenzene,
1-(thiocarbamyl)-3,5-bis(trifluoromethyl)benzene,
1-(thiocarbamyl)-3,5-dichlorobenzene,
1-(thiocarbamyl)-3,5-dimethoxybenzene,
1-(thiocarbamyl)-3,5-dimethylbenzene,
1-(thiocarbamyl)-3-(diethylamino)propane,
1-(thiocarbamyl)-3-(methylthio)benzene,
1-(thiocarbamyl)-3-(trifluoromethyl)benzene,
1-(thiocarbamyl)-3-acetylbenzene,
1-(thiocarbamyl)-3-benzyloxybenzene,
1-(thiocarbamyl)-3-bromobenzene,
1-(thiocarbamyl)-3-bromopropane,
1-(thiocarbamyl)-3-carboxybenzene,
1-(thiocarbamyl)-3-chloro-2-methylbenzene,
1-(thiocarbamyl)-3-chloro-4-fluorobenzene,
1-(thiocarbamyl)-(3-chloro-4-methylphenyl)methane,
1-(thiocarbamyl)-3-chloro-4-methylbenzene,
1-(thiocarbamyl)-(3-chlorophenyl)methane,
1-(thiocarbamyl)-3-chlorobenzene,
1-(thiocarbamyl)-3-chloropropane,
1-(thiocarbamyl)-3-cyanobenzene,
1-(thiocarbamyl)-3-dimethylaminopropane,
1-(thiocarbamyl)-3-ethoxycarbonylbenzene,

1-(thiocarbamyl)-3-ethylbenzene,
1-(thiocarbamyl)-(3-fluorophenyl)methane,
1-(thiocarbamyl)-3-fluorobenzene,
1-(thiocarbamyl)-3-iodobenzene,
1-(thiocarbamyl)-(3-methoxyphenyl)methane,
1-(thiocarbamyl)-3-methoxycarbonylbenzene,
1-(thiocarbamyl)-3-methoxybenzene,
1-(thiocarbamyl)-3-methoxypropane,
1-(thiocarbamyl)-3-methyl-2-butane,
1-(thiocarbamyl)-(3-methylphenyl)methane,
1-(thiocarbamyl)-3-methylbutane,
1-(thiocarbamyl)-3-morpholinopropane,
1-(thiocarbamyl)-3-nitrobenzene,
1-(thiocarbamyl)-3-pentane,
1-(thiocarbamyl)-3-phenylpropane,
3-(thiocarbamyl)pyridine,
1-(thiocarbamyl)-4-(benzyloxy)benzene,
1-(thiocarbamyl)-4-(dimethylamino)benzene,
1-(thiocarbamyl)-4-(methylthio)benzene,
1-(thiocarbamyl)-4-(trifluoromethoxy)benzene,
1-(thiocarbamyl)-4-(trifluoromethyl)benzene,
1-(thiocarbamyl)-4-acetylbenzene,
1-(thiocarbamyl)-4-bromo-2,6-dimethylbenzene,
1-(thiocarbamyl)-4-bromo-2-chlorobenzene,
1-(thiocarbamyl)-4-bromo-2-methylbenzene,
1-(thiocarbamyl)-4-bromo-2-trifluoromethylbenzene,
1-(thiocarbamyl)-4-bromobenzene,
1-(thiocarbamyl)-4-carboxybenzene,
1-(thiocarbamyl)-4-chloro-2-(trifluoromethyl)benzene
, 1-(thiocarbamyl)-4-chloro-2-methylbenzene,
1-(thiocarbamyl)-4-chloro-3-nitrobenzene,
1-(thiocarbamyl)-4-chloro-3-trifluoromethylbenzene,
1-(thiocarbamyl)-(4-chlorophenyl)methane,
1-(thiocarbamyl)-4-chlorobenzene,
1-(thiocarbamyl)-4-cyanobenzene,
1-(thiocarbamyl)-4-diethylaminobenzene,
1-(thiocarbamyl)-4-ethoxycarbonylbenzene,

1-(thiocarbamyl)-4-ethoxybenzene,
1-(thiocarbamyl)-4-ethylbenzene,
1-(thiocarbamyl)-4-fluoro-2-methylbenzene,
1-(thiocarbamyl)-(4-fluorophenyl)ethane ,
1-(thiocarbamyl)-(4-fluorophenyl)methane,
1-(thiocarbamyl)-4-fluorobenzene,
1-(thiocarbamyl)-4-iodobenzene,
1-(thiocarbamyl)-4-isopropylbenzene,
1-(thiocarbamyl)-4-methoxy-2-methylbenzene,
1-(thiocarbamyl)-4-methoxy-2-nitrobenzene,
1-(thiocarbamyl)-(4-methoxyphenyl)methane,
1-(thiocarbamyl)-4-methoxycarbonylbenzene,
1-(thiocarbamyl)-4-methoxybenzene,
1-(thiocarbamyl)-4-methyl-2-nitrobenzene,
1-(thiocarbamyl)-(4-methylphenyl)methane,
1-(thiocarbamyl)-4-n-butyl-2-methylbenzene,
1-(thiocarbamyl)-4-n-butylbenzene,
1-(thiocarbamyl)-4-nitrobenzene,
1-(thiocarbamyl)-4-phenoxybenzene,
1-(thiocarbamyl)-4-phenylazobenzene,
1-(thiocarbamyl)-4-phenylbutane,
1-(thiocarbamyl)-4-sulfamoylbenzene,
1-(thiocarbamyl)-4-tert-butylbenzene,
1-(thiocarbamyl)-5-chloro-2,4-dimethoxybenzene,
1-(thiocarbamyl)-5-chloro-2-methoxybenzene,
1-(thiocarbamyl)-5-chloro-2-methylbenzene,
1-(thiocarbamyl)-5-fluoro-2-methylbenzene,
1-(thiocarbamyl)-5-indane,
2-(thiocarbamyl)-5-norbornene,
2-(thiocarbamyl)-6-methylheptane,
9-(thiocarbamyl)acridine,
1-(thiocarbamyl)-2-propene,
1-(thiocarbamyl)-(1-phenyl)ethane,
1-(thiocarbamyl)-phenylmethane,
1-(thiocarbamyl)-cycloheptane,
1-(thiocarbamyl)-cyclohexylmethane,
1-(thiocarbamyl)-cyclohexane,

1-(thiocarbamyl)-cyclooctane,
1-(thiocarbamyl)-cyclopentane,
1-(thiocarbamyl)-cyclopropane, diethyl
L-2-thiocarbamyl-glutarate, dimethyl
L-thiocarbamyl-succinate, ethyl
2-thiocarbamylpropionate, ethyl
3-thiocarbamylbutyrate, ethyl
3-thiocarbamylpropionate, ethyl
4-thiocarbamylbutyrate, 1-(thiocarbamyl)-ethane,
ethyl thiocarbamylacetate,
1-(thiocarbamyl)-2-methylpropane,
1-(thiocarbamyl)-1-methylethane,
thiocarbamylacetaldehyde dimethyl acetal,
thiocarbamylphenyl sulfone,
1-(thiocarbamyl)-2-butene,
1-(thiocarbamyl)-methoxymethane, methyl
2-thiocarbamylacetate, methyl
2-thiocarbamylbenzoate, methyl
3-thiocarbamylpropionate,methyl
2-thiocarbamylbutyrate, methyl, methyl
L-2-thiocarbamyl-3-methyl-butyrate, methyl
L-2-thiocarbamyl-3-phenyl-propionate, methyl
L-2-thiocarbamyl-4-(methylthio)butyrate, methyl
L-2-thiocarbamyl-4-methylvalerate,
1-(thiocarbamyl)-pentane, 1-(thiocarbamyl)-butane,
1-(thiocarbamyl)-hexane, 1-(thiocarbamyl)-propane,
2-(thiocarbamyl)-norbornane,
1-(thiocarbamyl)-4-vinylbenzene,
1-(thiocarbamyl)-pentafluorobenzene,
1-(thiocarbamyl)-benzene, 1-(thiocarbamyl)-propyne
and 2-(thiocarbamyl)-butane.

13. A method for preparing the combinatorial library of claim 9, comprising:

(a) reacting one or more resin-bound amines with one or more nitrile-containing carboxylic acids, nitrile-containing isocyanates or nitrile-containing radicals with a leaving group to obtain two or more resin-bound nitriles;

(b) cyclizing the resin-bound nitriles to obtain oxadiazoles containing an amino-protected group; and

(c) deprotecting the amino-protected group to obtain oxadiazole a combinatorial library of two or more oxadiazole amine compounds.

14. The method of claim 13, further comprising step (d), reacting the oxadiazole amine compounds with one or more carboxylic acid, sulfonyl chloride, isocyanate or isothiocyanate containing compounds to obtain a combinatorial library of two or more oxadiazole compounds.

15. A method for preparing the combinatorial library of claim 9, comprising:

(a) reacting one or more resin-bound amines with one or more nitrile-containing carboxylic acids, nitrile-containing isocyanates or nitrile-containing radicals with a leaving group to obtain two or more resin-bound nitriles;

(b) cyclizing the nitriles to obtain oxadiazoles containing a leaving group; and

(c) reacting the leaving group with a primary amine or secondary amine to obtain a

combinatorial library of two or more oxadiazole secondary amine or oxadiazole tertiary amine compounds.

16. The method of claim 15, further comprising step (d), reacting the secondary oxadiazole amine compounds with one or more carboxylic acid, sulfonyl chloride, isocyanate or isothiocyanate containing compounds to obtain a combinatorial library of two or more oxadiazole compounds.

17. The method of claim 15, wherein the resin-bound amine is prepared by displacing a resin-bound leaving group with a primary amine.

18. The method of claim 15, wherein the resin-bound amine is prepared by reducing a resin-bound imine formed from either a resin-bound aldehyde with a primary amine or a resin-bound primary amine with an aldehyde.

19. A method for preparing the combinatorial library of claim 9, comprising:

(a) reacting one or more resin-bound leaving groups with one or more nitrile-containing phenoxide ions or amines to obtain two or more resin-bound nitriles;

(b) cyclizing the nitriles to obtain oxadiazoles containing an amino-protected group; and

(c) deprotecting the amino-protected group to obtain a combinatorial library of two or more oxadiazole compounds.

20. The method of claim 19, further comprising step (d), reacting the oxadiazole amine compounds with one or more carboxylic acid, sulfonyl chloride, isocyanate or isothiocyanate containing compounds to obtain a combinatorial library of two or more oxadiazole compounds.

21. A method for preparing the combinatorial library of claim 9, comprising:

(a) reacting one or more resin-bound leaving groups with one or more nitrile-containing phenoxide ions or amines to obtain two or more resin-bound nitriles;

(b) cyclizing the nitriles to obtain oxadiazoles containing a leaving group; and

(c) reacting the leaving group with a primary amine or secondary amine to obtain a combinatorial library of two or more oxadiazole secondary amines or oxadiazole tertiary amines.

22. The method of claim 21, further comprising step (d), reacting the secondary oxadiazole amine compounds with one or more carboxylic acid, sulfonyl chloride, isocyanate or an isothiocyanate containing compounds to obtain a combinatorial library of two or more oxadiazole compounds.

23. A method for preparing the combinatorial library of claim 9, comprising:

(a) reducing an imine formed between one or more resin-bound aldehydes and one or more

amines containing a protected carboxylic acid to obtain two or more protected carboxylic acids bound to resin;

(b) deprotecting the protected carboxylic acids to obtain resin bound carboxylic acids; and

(c) reacting the resin bound carboxylic acids with one or more amidoxime containing compounds to obtain a combinatorial library of two or more oxadiazole compounds.

24. A method for preparing the combinatorial library of claim 9, comprising:

(a) reacting one or more resin-bound alcohols with one or more amines containing a protected carboxylic acid to obtain two or more protected carboxylic acids bound to resin through a carbamate linkage;

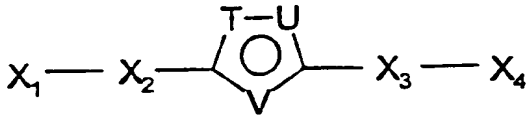
(b) deprotecting the resin-bound protected carboxylic acids to obtain resin bound carboxylic acids; and

(c) reacting the resin-bound carboxylic acids with one or more amidoxime containing compounds to obtain a combinatorial library of two or more oxadiazole compounds.

AMENDED CLAIMS

[received by the International Bureau on 31 March 2000 (31.03.00);
original claim 1 amended; new claims 25-27 added; remaining claims unchanged (11 pages)]

1. A single compound of the structure:



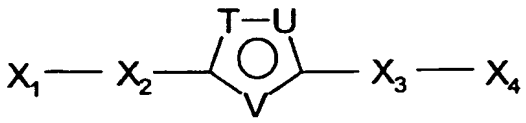
Formula (I)

wherein:

T, U and V are independently selected from an oxygen, sulfur or nitrogen atom, provided that at least two of T, U and V are a nitrogen atom;

X_1 is selected from the group consisting of $-NHC(O)NR_1R_2$, $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$, and $-CH_2NR_1R_2$, wherein R_1 is a hydrogen atom or a functionalized resin, and R_2 is a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, the formulae:

25. A single compound of the structure:

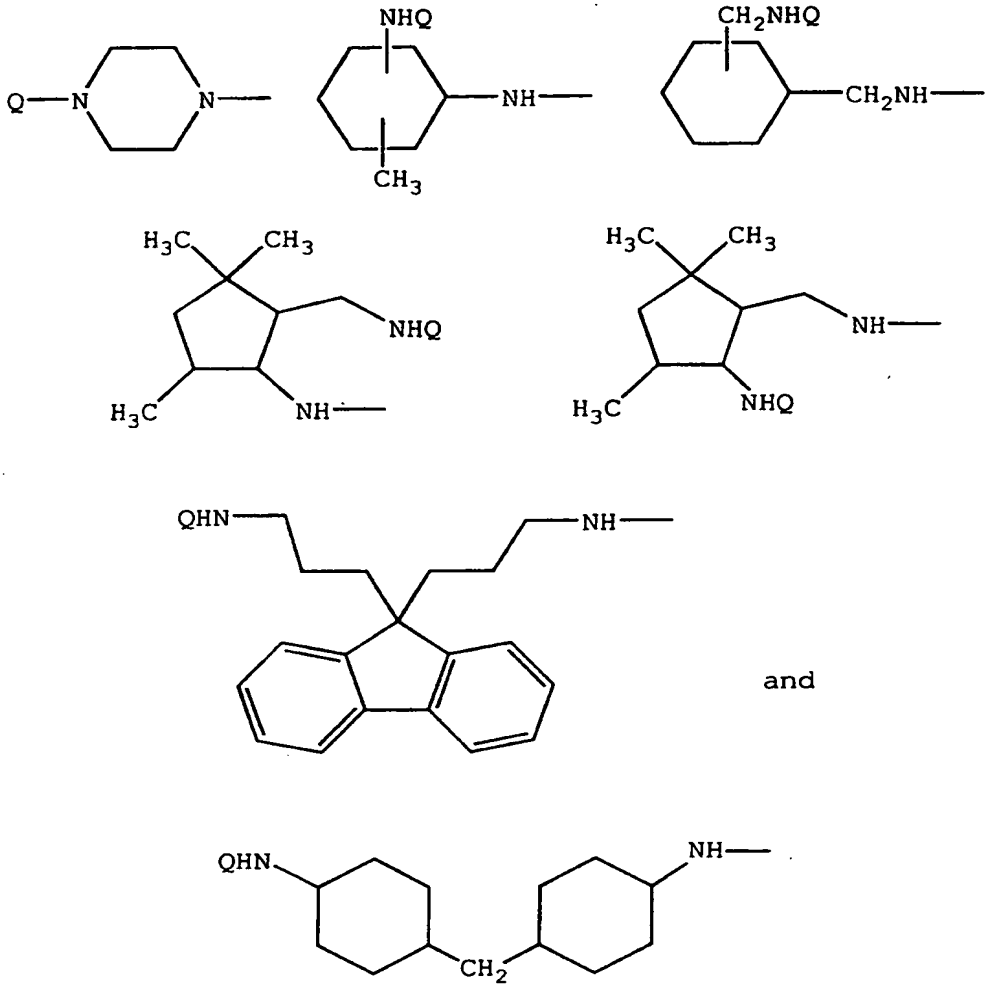


Formula (I)

wherein:

T, U and V are independently selected from an oxygen, sulfur or nitrogen atom, provided that at least two of T, U and V are a nitrogen atom;

X_1 is selected from the group consisting of H, $-NHC(O)NR_1R_2$, $-CO_2R_1$, $-OR_1$, $-NR_1R_2$, $-C(O)NR_1R_2$, and $-CH_2NR_1R_2$, wherein R_1 is a hydrogen atom or a functionalized resin, and R_2 is a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 substituted alkenyl, phenyl, substituted phenyl, naphthyl, substituted naphthyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, heteroaryl, substituted heteroaryl, heterocycle, substituted heterocycle, the formulae:



and

wherein Q is a hydrogen atom or functionalized resin;

X_2 is selected from the group consisting of C_1 to C_{12} alkylene, C_1 to C_{12} substituted alkylene, C_2 to C_7 alkenylene, C_2 to C_7 substituted alkenylene, C_2 to C_7 alkynylene, C_3 to C_7 cycloalkylene, C_3 to C_7 substituted cycloalkylene, C_5 to C_7 cycloalkenylene, C_5 to C_7 substituted cycloalkenylene, phenylene, substituted phenylene, naphthylene, substituted naphthylene, C_7 to C_{12} phenylalkylene, C_7 to C_{12} substituted phenylalkylene,

the formula:

$-(CH_2)_m-G-(CH_2)_n-$

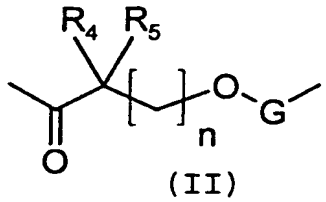
wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and G is selected from phenylene and substituted phenylene,

the formula:

$-(CH_2)_m-NR_3-(CH_2)_n-$

wherein m and n are integers independently selected from 0 to 6, provided that m and n are not together 0; and R_3 is selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_1 to C_4 alkyl sulfonyl, C_1 to C_4 substituted alkyl sulfonyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl, substituted phenylaminothiocarbonyl, C_1 to C_7 alkoxycarbonyl, C_1 to C_7 substituted alkoxycarbonyl, phenoxycarbonyl and substituted phenoxycarbonyl,

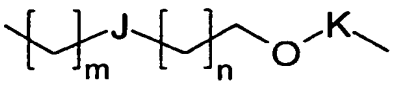
the formula:



(II)

wherein n is an integer selected from 0 to 6; R_4 and R_5 are together or independently a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl and protected hydroxymethyl; and G is selected from phenylene and substituted phenylene, and

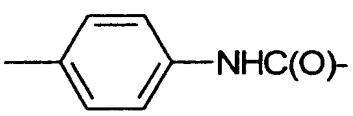
the formula:



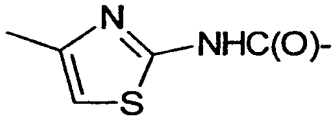
(III)

wherein J and K are each selected from the group consisting of phenylene and substituted phenylene, and m and n are independently selected from 0 and 1, and

the formulae (IV) and (V):

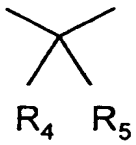


(IV)



(V) ; and

X_3 is absent or is selected from the group consisting of the formula:

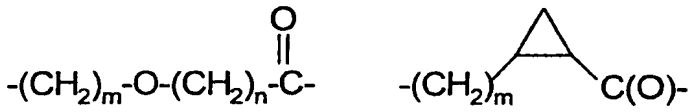


wherein:

R_4 and R_5 are together or independently selected from the group consisting of a hydrogen atom, C_1 to C_6 alkyl, C_2 to C_7 alkenyl, C_2 to C_7 alkynyl, C_1 to C_6 substituted

alkyl, C_2 to C_7 substituted alkenyl, C_2 to C_7 substituted alkynyl, C_1 to C_7 acyl, C_1 C_7 substituted acyl, C_3 to C_7 cycloalkyl, C_3 to C_7 substituted cycloalkyl, C_5 to C_7 cycloalkenyl, C_5 to C_7 substituted cycloalkenyl, a heterocyclic ring, substituted heterocyclic ring, heteroaryl, substituted heteroaryl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy, phenyl, substituted phenyl, naphthyl, substituted naphthyl, cyclic C_2 to C_7 alkylene, substituted cyclic C_2 to C_7 alkylene, cyclic C_2 to C_7 heteroalkylene, substituted cyclic C_2 to C_7 heteroalkylene, carboxy, protected carboxy, hydroxymethyl and protected hydroxymethyl,

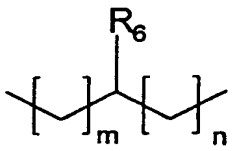
the formulae (VIa) and (VIb):



(VIa) (VIb)

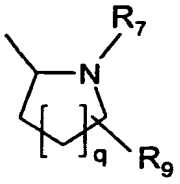
wherein in formula (VIa) m and n are independently selected from 0, 1, 2, 3 and 4; and wherein in formula (VIb) m is selected from 0, 1, 2, 3 and 4;

the formula:

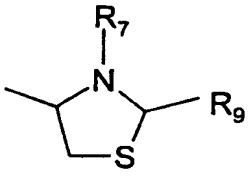


wherein R_6 is selected from the group consisitng of a hydrogen atom, amino, amino-protecting group, $-NR_7R_8$, carboxy, carboxy-protecting group, $-C(O)NR_7R_8$, wherein R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and m and n are independently selected from 0, 1, 2, 3 and 4; and

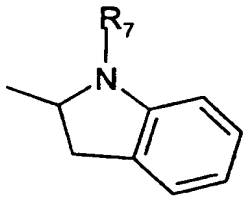
the formulae (VII) to (XIII):



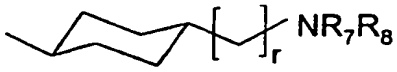
(VII)



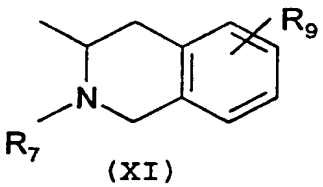
(VIII)



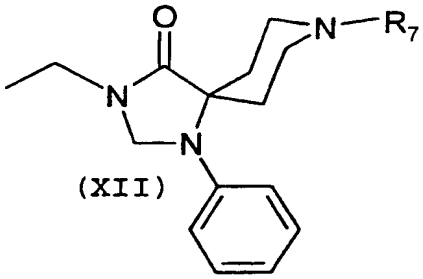
(IX)



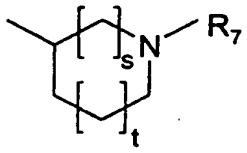
(X)



(XI)



(XII)



(XIII)

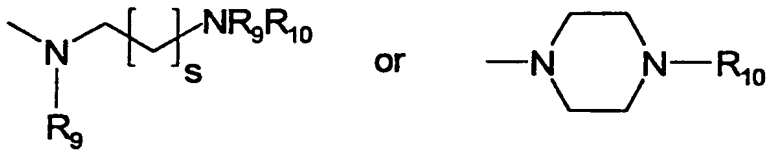
wherein q is 1 or 2; r is 0 or 1; s and t are independently selected from 0, 1 or 2; and R_7 and R_8 are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl,

C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and

R_9 is selected from a hydrogen atom, -OH, hydroxy-protecting group, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_1 to C_7 alkoxy, C_1 to C_7 phenylalkoxy, phenyl, substituted phenyl, heteroaryl and substituted heteroaryl; and

X_4 is absent or is selected from the group consisting of a hydrogen atom, -OH, $-CO_2H$, $-C(O)NR_7R_8$ and $-NR_7R_8$, wherein R_7 and R_8 are independently selected from a functionalized resin, a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl,

and the formulae:



wherein R_9 and R_{10} are independently selected from a hydrogen atom, C_1 to C_6 alkyl, C_1 to C_6 substituted alkyl, C_7 to C_{12} phenylalkyl, C_7 to C_{12} substituted phenylalkyl, C_7 to C_{12} phenylalkoxy, C_7 to C_{12} substituted phenylalkoxy C_1 to C_7 acyl, C_1 to C_7 substituted acyl, phenylsulfonyl, substituted phenylsulfonyl, C_1 to C_4 alkylsulfonyl, C_1 to C_4 substituted alkylsulfonyl, C_1 to C_6 alkylaminocarbonyl, C_1 to C_6 substituted alkylaminocarbonyl, phenylaminocarbonyl, substituted phenylaminocarbonyl, C_1 to C_6 alkylaminothiocarbonyl, C_1 to C_6 substituted alkylaminothiocarbonyl, phenylaminothiocarbonyl and substituted phenylaminothiocarbonyl; and s is an integer selected from 1 to 5;

a pharmaceutically acceptable salt of a compound thereof; or

a biologically active ester form of a compound thereof.

26. The single compound of claim 25, wherein one of T, U and V is oxygen and the other two positions are each nitrogen.

27. The single compound of claim 26, wherein U is oxygen, T is nitrogen and V is nitrogen.

Fig. 1

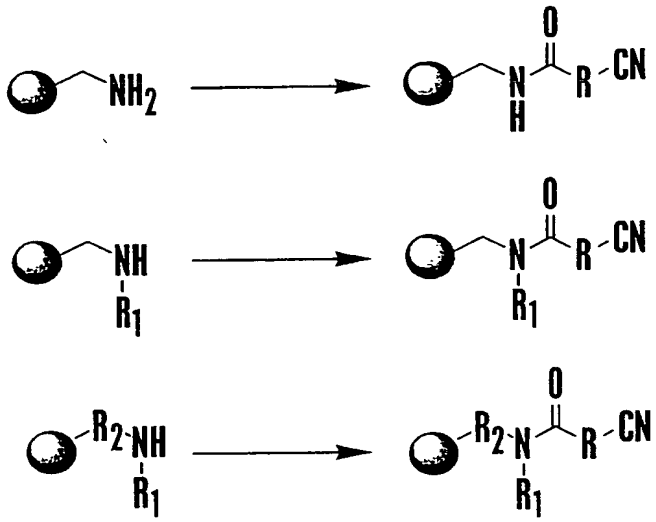


Fig. 2

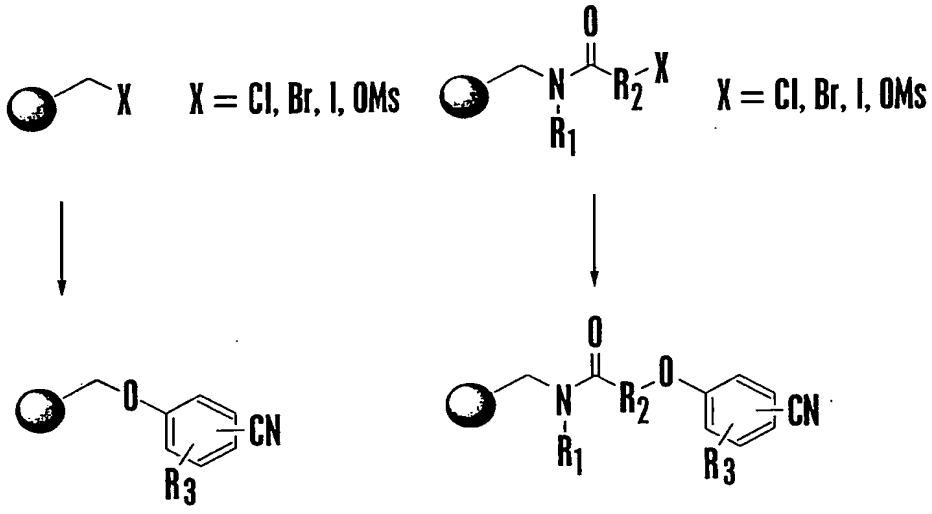
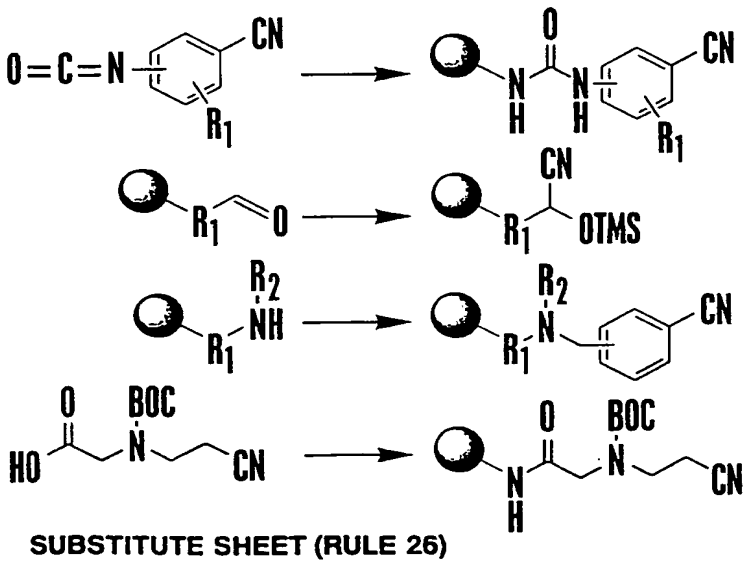


Fig. 3



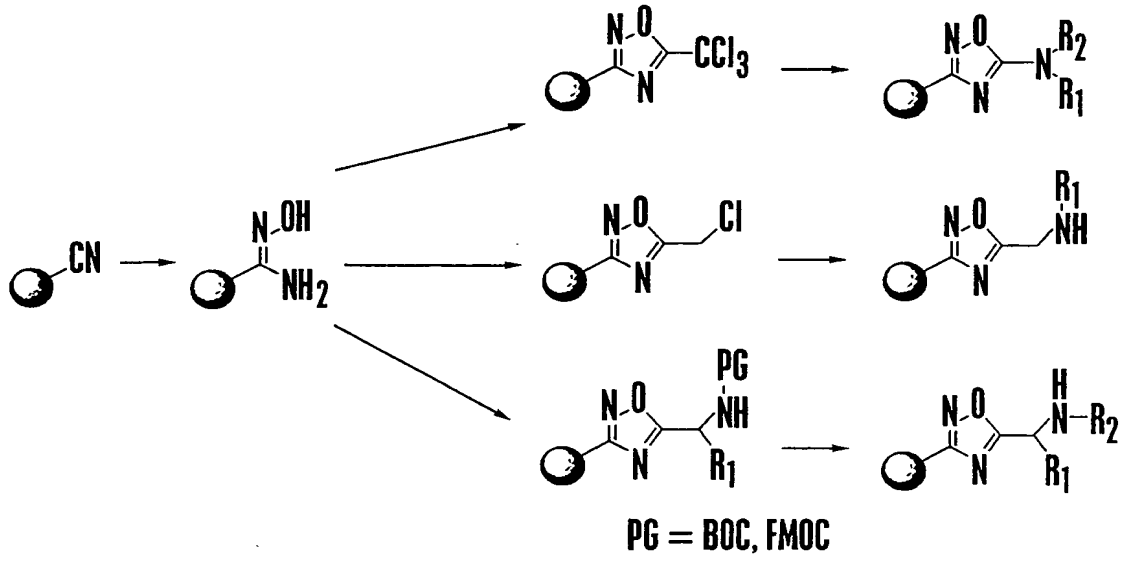
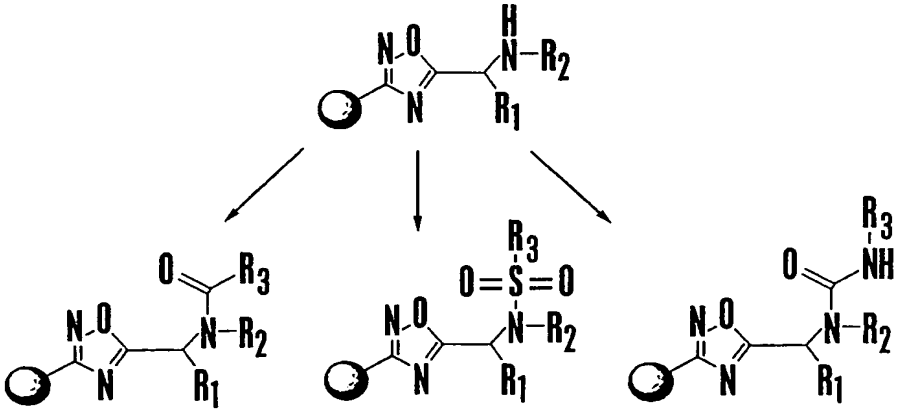


Fig. 4

Fig. 5



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/25331

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61K 31/075, 31/10; C07D 9/62, 271/06, 271/10
US CL :435/ 6, 7.1; 530/333, 334; 548/119, 131, 132, 133
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/ 6, 7.1; 530/333, 334; 548/119, 131, 132, 133

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X - Y	US 4,929,628 A (MCARTHUR et al) 29 May 1990, see entire document.	1-12 --- 13-24
X - Y	US 5,242,890 A (CHO et al.) 07 September 1993, see entired document.	1-12 --- 13-24
Y	GORDON et al. Applications of Combinatorial Technologies to Drug Discovery. 2. Combinatorial Organic Syntheses, Library Screening Strategies, and Future Directions. J. Med. Chem. 13 May 1994, Vol. 37, No. 10, pages 1385-1401, see entire article, especially page 1386.	13-24

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

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"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
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Date of the actual completion of the international search 18 JANUARY 2000	Date of mailing of the international search report 14 FEB 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer BENNETT CELSA Telephone No. (703) 308-0196

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/25331

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LIANG et al. An Improved Oxadiazole Synthesis Using Peptide Coupling Agents. Tetrahedron Letters. 09 September 1996, Vol. 37, No. 37, pages 6627-6630, see entire article.	13-24

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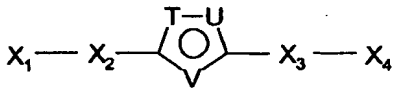
(54) Title: OXADIAZOLE, THIADIAZOLE AND TRIAZOLE DERIVATIVES AND COMBINATORIAL LIBRARIES THEREOF



(I)

(57) Abstract

The present invention relates to novel compounds of formula (I) wherein X_1, X_2, X_3, X_4, T, U and V have the meanings provided. The invention further relates to combinatorial libraries containing at least two or more such compounds, and to methods of preparing combinatorial libraries composed of such compounds.

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International application No.
PCT/US99/25331

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) :A61K 31/075, 31/10; C07D 271/06, 271/10
US CL :435/ 6, 7.1; 530/333, 334; 548/119, 131, 132, 133
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

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